Cardiology VOLUME 3: *Clinical Cardiology*

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CARDIOLOGY

An Encyclopedia of the Cardiovascular System

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Foreword

This work is at once a landmark in clinical cardiology and an indication of the Golden Age of Medicine in which we now live. Because wondrous things have become commonplace, we can appreciate this age only in retrospect. From rude beginnings it is possible to trace, over the centuries of recorded history, the gradual refinement in skills, the slow accumulation of factual knowledge, and the emergence of a scientific discipline so essential to success in the walks of science. Progress, painfully slow and often faltering till late in the nineteenth century, then began to accelerate at an ever-increasing rate. Within the memory of some now living, individual triumphs in scattered departments of science combined in one mighty triumphant flourish to usher in the modern era. Epidemics, once the scourge of man, were abolished, certain diseases, once relentless in their course, were controlled, old age, once a rarity, became the rule. It is unlikely that within a comparable period of time man will ever again repeat the stupendous feat of doubling his span of life.

Cardiologists, while sharing in these triumphs, saw heart disease assume the lead as a cause of death in many countries. Thus, although gratified by the increased longevity of man, we are nevertheless challenged by the disclosure that the cardiovascular system is now the weakest strand in the thread of life. Indeed, its relative importance in the lives of men appears destined to increase, for there is nothing in sight pointing to a major break-through in the prevention of heart disease in old age.

In sponsoring this encyclopedia, the American College of Cardiology, dedicated to the continuing education of its membership, is simply fulfilling one of its obligations That this particular obligation weighed more heavily on the minds of some of its officers than on others raised the question of the relative merits of different methods of postgraduate education We cannot here record the deliberations which finally led to approval of this undertaking, but they reflected the need for putting on record the widening horizons of our knowledge of cardiovascular disease

That the presentation of information concerning the heart and circulation requires four volumes involving upwards of 250 authors has important implications It is evidence that narrowing of interest and progress go hand in hand, and that subdivision within the field of cardiology is well established But this subdivision, so essential for progress, must be reconstituted for those whose clinical responsibilities cover a broad area In effect this encyclopedia represents such a reconstitution It contains authoritative information abstracted from an immense mass of medical literature which could not be reviewed effectively by an individual. The organization of this material is based on a logical framework

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Preface

This work was started as a result of a bold and far-sighted initiative of Dr. Ashton Graybiel, then president of the American College of Cardiology.

The task of editing an encyclopedia of cardiology represents a challenge which is both appealing and frightening.

Among the multitude of books of cardiology which have been published in the last 20 years, the majority belongs to the type of the medium-sized, monographic textbook written by a single author. A few have been written in collaboration by several authors. These, however, do not attempt to be complete and are, moreover, too unsystematic to be helpful Being of the "fixed-volume" type, they are soon outdated and, therefore, forgotten.

In ancient Greece, *encyclopaedia* meant "instruction in the whole circle, or complete system of learning." In a more restricted sense, encyclopedia means "a system or classification of various branches of knowledge, a subject on which many books have been published" While many encyclopedias of the past have been of the "alphabetical type" (each word to be explained is listed in alphabetical order), others have tried to reconcile system with completeness. Thus, even in the early editions of the *Encyclopaedia Britannica,* the various sciences and arts (such as anatomy or surgery) were "digested into distinct treatises or systems" On the other hand, technical terms were explained in alphabetical order Older encyclopedias, like Plinius's *Natural History* of the year 77 A.D. (37 books with 2,493 chapters) or *Yung-Lo Ta Tien*, the Chinese encyclopedia of 1403 A D (11,095 volumes prepared in four years by over 2,000 scholars), were developed according to system The latter even included well-known books reproduced without change.

In the opinion of the editor, a modern encyclopedia of cardiology ought to have the following characteristics: (1) It should encompass all available knowledge on the heart and vessels, including history, embryology, anatomy, physiology, physical and technical methods of examination, bacteriology and pa- [illegible] , and [illegible] , thus [illegible] consultation. [illegible] It should be of the loose-leaf type, in order to keep abreast of medical progress It is then possible that some of the readers may prefer to call this a *treatise.*

The principle of extending the work to all kinds of knowledge in the cardiovascular field should not be carried too far in the marginal fringes of medical or technical sciences This process would divert and distract the attention of the reader and would render consultation too difficult [illegible]

which constitutes a resynthesis of the important elements in the field of cardiology.

In using this encyclopedia, the physician must let go of his inclination to be taught, and cultivate the art of selecting new items of information and fitting them into a frame of reference dictated by his needs. This method does require a capacity for mental independence and is effective only in so far as this is exhibited by those for whom the encyclopedia is intended. Admittedly a work of this sort represents a form of communication in which there is much redundancy. At what point will the evil of redundancy equal or exceed the good contained in the message? Herein lies a very real problem with which we should be concerned in the future.

It is noteworthy that in the compilation of this work we are more dependent upon an editor than upon an author. The choice of Dr. Luisada to edit the work has been fortunate. He has exhibited not only a natural talent for this task but also the quality of persevering in the face of difficulties. To him alone belongs the credit for bringing the encyclopedia to fruition. The present handbook must be regarded as a monument to his genius

ASHTON GRAYBIEL

2. Selection of persons with diversified knowledge (physiology, pathology, pediatrics, surgery, etc.), so that all fields may be covered by competent editors.

3. Choice of as many young scientists as possible, in order to have a high potential of enthusiasm, criticism, and working capacity.

The final product will reveal whether these directives are sound and have been followed as closely as possible.

The publication of this encyclopedia was made possible by the continued support of the American College of Cardiology through the action of its board of trustees, by generous contributions of five pharmaceutical houses, and by the *warm collaboration of the McGraw-Hill Book Company, Inc., Blakiston Division.*

ALDO A. LUISADA
Editor in Chief

cardiology. It is likely that a four-volume, 5,000-page encyclopedia would represent the optimal size. However, practical considerations indicate a more limited approach for the first version. Therefore, a four-volume, 3,600-page size is considered for the first edition, even though gradual revision and extension over the following ten years will probably increase the size to that previously mentioned.

Several titles have been considered for this encyclopedia. The one preferred by the editor, *Encyclopedia of Cardiology,* has been discarded for fear of discouraging prospective readers. The more modest title which has been selected—*Cardiology*—emphasizes the main scope [knowledge about the heart (and vessels)] even though it has a more modest sound than the original title. The titles of the four volumes have been selected on the basis of their content.

The problem of correlation has been the rock on which many textbooks written by multiple authors have foundered. If the various parts do not follow a logical sequence; if some of them are disproportionately long or short; if some are written by obscure authors of poor talent while others are the result of the work of well-known authorities, then the whole encyclopedia has no value.

In order to obviate these possibilities, the following steps are necessary: (1) the authors selected should be among the best, (2) each should receive a carefully selected and clearly outlined job, and (3) the editors should be able to refuse, abbreviate, or send back for correction any received text. Therefore, courage, patience, and hard labor are necessary to ensure a successful literary production.

The outcome of the work depends to a large extent upon the selection of authors. Well-known authors who have left a mark in the history of cardiology are the natural choice. However, they may be reluctant to undertake a major task and, moreover, may not be able to ensure continuity on account of their age. A compromise may be represented by asking these authors to prepare the text in collaboration with one of their associates The associate would be the natural choice for any future revision of the text. However, a different author may entirely revise a chapter at a future date.

Science is international. If a truly objective work is to be published, authors of all nationalities should be asked to contribute. The recent tremendous progress of cardiology in the North American continent may require that a majority of the authors be selected in the United States and Canada However, numerous contributors have been selected from England, continental Europe, Mexico, South America, Africa, and Asia, so that a truly "global" representation of cardiology may result.

How much of the text should reflect generally accepted viewpoints; how much should present new ideas still awaiting confirmation? This problem cannot be solved in a general way. The viewpoint of the editor is that an intermediate position should be preferred. Texts reflecting only generally accepted views might render the entire work obsolete within a few years. On the other hand, many new viewpoints cannot withstand the test of time and are gradually discarded. Whatever the error, whether in the sense of conservatism or in that of progressivism, a loose-leaf type of work may remedy it more rapidly than any standard type of volume.

The Editorial Board has been selected with great care according to these viewpoints:

1. Inclusion of a few authorities which would help in laying down the directives of the work.

2. Selection of persons with diversified knowledge (physiology, pathology, pediatrics, surgery, etc.), so that all fields may be covered by competent editors.

3. Choice of as many young scientists as possible, in order to have a high potential of enthusiasm, criticism, and working capacity.

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PART 10. CORONARY HEART DISEASE

1

Classification of heart disease[1]

LOUIS H. SIGLER

Diseases of the heart occur in various forms and degrees of structural and functional abnormalities in different individuals The underlying causes likewise vary greatly in different cases For these reasons it is essential to have a clear classification of such diseases as to their underlying etiology, structural abnormalities, and functional derangements, as well as of the disturbances in rate and rhythm

ETIOLOGIC CLASSIFICATION

Disturbances and diseases of the heart may be caused by intrinsic local or general constitutional diseases and by extrinsic factors.

Constitutional Diseases

1 Arteriosclerosis

2 Hypertension, with or without coronary atherosclerosis

3 Rheumatic fever

4. Disturbances of the nervous system

(a) Psychosomatic

(b) Neurocirculatory

(c) Reflexes from other diseased viscera

(d) Reflexes from vascular sensory receptor innervations (especially the carotid sinus)

5 Endocrine disease

(a) Hyperthyroidism

(b) Hypothyroidism

(c) Adrenocortical hypofunction

(d) Hypoinsulinism

6. Blood dyscrasias

(a) Primary and secondary anemias

(b) Various leukemias

7. Metabolic diseases usually associated with arteriosclerosis

(a) Diabetes mellitus

(b) Gout

(c) Obesity

8 Pulmonary arterial hypertension

(a) Essential

(b) Secondary to severe chronic pulmonary disease

(c) Due to an acute massive pulmonary embolization

9 Neoplastic disease

(a) Primary

(b) Metastatic

(c) As an extension from adjacent structures

10 Collagen diseases

11. Congenital anomalies

(a) Due to maldevelopment

(b) Due to fetal infection in intrauterine life (rare)

Extrinsic Factors

1. Infections

(a) Bacterial—various types and strains of bacteria

(b) Spirochetal, most frequent is syphilis

(c) Parasitic—(*Plasmodium malariae*, *Echinococcus*, *trichina*)

2 Intoxications

[1] It is obvious that any classification reflects the viewpoints of the writer For this reason, Sigler's classifications may differ from those of the writers of subsequent clinical chapters. Considering the number of authors, no attempt to obtain a unity of concepts in the field of classification has been made Editor

(*a*) Drugs and chemicals—digitalis, quinidine, carbon monoxide, and others
(*b*) Bacterial toxins, as in diphtheria

3. Severe trauma penetrating and nonpenetrating chest or bodily injuries or severe strain—*extrinsic* (physical) or *intrinsic* (due to fluctuations in circulatory dynamics)
4. Vitamin B deficiency

It should be understood that the real underlying causes of heart diseases vary greatly and are largely unknown Hereditary predisposition, climate, diet, strain, lack of rest, and many other factors undoubtedly play their part. Although arteriosclerosis, for instance, is considered as the cause of arteriosclerotic heart disease, the main underlying causes of arteriosclerosis itself are still shrouded in mystery. The same is true of the other most important causes.

STRUCTURAL CLASSIFICATION

Structural diseases of the heart may be divided into the following five main groups (1) inflammatory, (2) degenerative, (3) traumatic, (4) alteration in size and shape, (5) neoplastic. Inasmuch as the congenital diseases present certain characteristic pathologic and clinical abnormalities, that group will be dealt with separately.

Inflammatory involvement may affect any part of the heart, the coronary vessels, the aorta, and the pulmonary artery It is usually not limited to one area, but some areas are more greatly involved than others. Depending upon the area of predominance of inflammation, there are:

1. Endocarditis
   (*a*) Acute, subacute, and chronic
   (*b*) Mural or valvular (valvulitis)
   (*c*) Rheumatic, bacterial, nonbacterial or indeterminate, verrucose (Libman-Sacks disease)
2. Myocarditis
   (*a*) Acute
   (*b*) Chronic, with continuous or frequently recurring activity
3. Pericarditis
   (*a*) Acute—fibrinous, serofibrinous, or purulent
   (*b*) Chronic, usually tuberculous or rheumatic
4. Coronary arteritis, part of general arteritis· rheumatic, due to thromboangiitis obliterans, periarteritis nodosa
5. Aortitis: syphilitic, rheumatic, bacterial
6. Pulmonary arteritis: syphilitic, rheumatic, bacterial, tuberculous, parasitic

Degenerative lesions may be divided into *chronic* and *acute*. Some of the former do not differ to any great extent from the end results of unresolved organized inflammatory processes and will be dealt with together.

Chronic Degenerative Lesions

1. Atherosclerosis
   (*a*) Coronary arteries
   (*b*) Aorta
   (*c*) Pulmonary artery
2. Pericardial and pleuropericardial
   (*a*) Fibrosis
   (*b*) Adhesions
   (*c*) Calcification
3. Myocardial
   (*a*) Fibrosis—patchy and diffuse, or massive and localized
   (*b*) Aneurysm
   (*c*) Fatty infiltration
4 Endocardial and valvular
   (*a*) Fibrosis, with or without calcification
   (*b*) Valvular defects—mitral stenosis and/or insufficiency, aortic stenosis and/or insufficiency, pulmonic stenosis and/or insufficiency, tricuspid stenosis and/or insufficiency
5 Scleroderma heart

Acute Degenerative Lesions

1 Coronary subintimal hemorrhage
2 Coronary occlusion—thrombotic, nonthrombotic, and embolic
3 Myocardial ischemia and ischemic necrosis, disseminated
4 Myocardial infarction
5 Mural endocardial thrombosis, of the atrial or ventricular chambers
6 Granular, hyaline, and fatty degeneration due to toxic factors or other causes

Traumatic Lesions

1 Penetrating lacerations of heart and vessels
2 Contusions and nonpenetrating lacerations
3 Myocardial infarction
4 Rupture of any of the valves
5. Tear of the chordae tendineae

6. Rupture of an aneurysm—cardiac, aortic, or pulmonic

7. Dissecting hematoma of the aorta (dissecting aneurysm)

8. Rupture of any of the chambers of the heart, of the aorta, or of the pulmonary artery

Alterations in the size of the heart and large vessels may consist of *hypertrophy, dilatation,* and *atrophy*

Cardiac hypertrophy and/or dilatation may affect.

1 The left or right atrium or ventricle

2 Both atria and/or both ventricles in various proportions

Hypertrophy and dilatation of the aortic or pulmonary arterial wall may be diffuse or saccular

Atrophy of the heart and great vessels may occur in some cases of senility or wasting diseases

Neoplasms of the heart may be *primary* or *metastatic*. *Primary tumors are very rare* They may originate in the endocardium, myocardium, or pericardium as myomas, fibromas, or cysts Metastatic tumors are somewhat more frequent.

DISTURBANCES OF RATE AND RHYTHM

Disturbances in the heart rate and rhythm may occur in structurally normal hearts, although the severe arrhythmias usually occur in the presence of organic heart disease Many of the disturbances may be diagnosed by physical examination, others require electrocardiographic studies for proper diagnosis

The following classification is based on the focus of origin of the impulse in the heart.

Disturbances in the Sinus Node

1 Sinus bradycardia
2 Sinus tachycardia
3 Sinoatrial standstill
4 Sinus arrhythmia

Interruption of Sinus Rhythm by Ectopic Impulses, Origin May Be

1 Atrial
2 Nodal
3 Ventricular

Displacement of the Pacemaker

1 Without tachycardia
    (*a*) Nodal rhythm
    (*b*) Shifting or wandering pacemaker
    (*c*) Double pacemaker and parasystole with interference dissociation
2. With tachycardia
    (*a*) Paroxysmal tachycardia (ectopic tachycardia)—atrial, nodal; ventricular; indeterminate
3. Flutter and fibrillation—atrial; ventricular

Conduction Disturbances

1. Atrioventricular block
    (*a*) Simple delay
    (*b*) Delay with dropped ventricular beats (periodic block)
    (*c*) Complete block
2. Bundle branch block
    (*a*) Partial or incomplete
    (*b*) Complete—left, right, indeterminate
3 Electrical alternans

FUNCTIONAL CLASSIFICATION

Included here are not only the functional disturbances of the heart itself but also those of the peripheral circulation. These may be classified into four main headings. (1) *myocardial,* (2) failure of the coronary circulation, (3) peripheral vascular failure, and (4) failure of the cerebral circulation.

Myocardial failure varies in degree *It may* affect the *left ventricle* in aortic valvular disease, mitral insufficiency, systemic hypertension, and other conditions, throwing a greater burden on that ventricle It may affect the *right ventricle* in mitral stenosis, pulmonary valvular disease, and other conditions, placing a greater strain on that ventricle, or as a sequela of prolonged left ventricular failure. It may affect *both ventricles* in arteriosclerotic heart disease without hypertension, in prolonged severe arrhythmia, multiple rheumatic valvular diseases, and diffuse myocardial diseases.

Failure of the coronary circulation may be *transient*, induced by strain or effort in the presence of coronary atheromatosis, *or it may* be *prolonged* The effects *may be* temporary or prolonged myocardial ischemia, resulting in ischemic necrosis *and diffuse* infarction. *Acute* failure in a localized area *of the* heart may be caused by sudden coronary occlusion or by hemodynamic factors The result most often is myocardial infarction of the area affected.

Peripheral vascular failure due to any cause may be so severe as to

nous return to the heart is decreased due to widespread arteriocapillary dilatation and emptying of the venous system. This may result in cessation of the circulation.

Failure of the cerebral circulation, if not due to local causes, may be induced by *cardiac arrest* due to sinoatrial block, ventricular asystole (in atrioventricular block), ventricular fibrillation, or severe peripheral vascular failure. An occasional condition which may precipitate any of these mechanisms and result in cerebral manifestations is the *carotid sinus syndrome.*

The classification of patients as to *degree* of functional damage is based upon the reaction of any given individual to his usual activities. This depends not only upon the functional state of the heart but also upon extrinsic factors such as individual sensitivity, variations in psychologic reaction to disease, variations in subjective manifestations, and differences in work experiences and training previous to the onset of heart disease. A classification based on *reaction to physical activity* as a test of the functional capacity of the heart is, therefore, largely conjectural. Nevertheless, we may roughly divide the various degrees of functional incapacity into the following four classes, as adopted by the American Heart Association.

Class I. Patients with heart disease who can carry on normal physical activity.

Class II. Patients in whom normal physical activity brings about moderate subjective and objective disturbances.

Class III. Patients in whom less than ordinary physical activity brings about marked disturbances but who are still comfortable at rest.

Class IV. Patients in whom disturbances occur even at rest.

CONGENITAL CARDIOVASCULAR DISEASES

Congenital cardiovascular diseases may be divided into three main groups: (1) acyanotic, (2) with late cyanosis (cyanose tardive), and (3) cyanotic.

Acyanotic Group. Here there is no abnormal communication between the pulmonic and systemic circulations and therefore no mixture of systemic venous and arterial blood. Many varieties of abnormalities occur in this group, the following are the most common:

1. Primary cardiac and valvular involvement
   (*a*) Dextrocardia
   (*b*) Aortic valvular or infundibular stenosis
   (*c*) Bicuspid aortic valve
   (*d*) Supernumerary aortic cusps
   (*e*) Pulmonary valvular or infundibular stenosis
   (*f*) Malformations of the tricuspid valve
   (*g*) Congenital cardiac hypertrophy
2. Abnormalities of the aorta
   (*a*) Double aortic arch
   (*b*) Right aortic arch
   (*c*) Coarctation of the aorta (infantile and adult types)
   (*d*) Congenital aneurysm of the sinus of Valsalva
3. Primary dilatation of the pulmonary artery
4. Draining of the pulmonary veins into the right atrium or the superior vena cava

Late Cyanosis (cyanose tardive). Here there is a direct shunt or communication between the systemic venous and arterial systems. Under normal conditions, because of the greater pressure in the systemic than in the pulmonic side of the systems, the abnormal flow of blood through the defect is in a direction from the former to the latter, and therefore there is no cyanosis. Under conditions of strain or when a greater burden is placed on the right ventricle, the pressure on the venous side suddenly becomes greater than on the arterial side and the blood flow through the defect is in a direction from the venous to the arterial side, resulting in cyanosis. Abnormalities belonging to this group are:

1. Patent ductus arteriosus
2. Defects of the interatrial septum
   (*a*) Marked patency of the foramen ovale
   (*b*) Persistent ostium primum
   (*c*) Atrial defect plus congenital or acquired mitral stenosis (Lutembacher's *syndrome*)
3. Patent interventricular septum
4. Patent aortic septum (usually in right sinus of Valsalva leading into pulmonary conus)

Cyanotic Group. Here there is a great variety in the form and degree of defects In many

cases a permanent venoarterial shunt exists. In some, no such shunt is present but there is a serious congenital cardiac defect which slows the circulation and results in chronic alterations in the capillary loops in various parts of the body, most marked in the fingers and toes, producing marked *clubbing*. The pathologic alterations of the pulmonary circulation, plus the effect of shunts, plus changes of the systemic capillaries and polycythemia result in deficient oxygenation of the blood and the cyanosis

The common conditions presenting a *permanent shunt* are

1 Tetralogy of Fallot· a combination of interventricular septal defect, dextroposition of aorta, pulmonic valvular or infundibular stenosis, and right ventricular hypertrophy

2 Eisenmenger's complex same as above except for the absence of pulmonary stenosis and the occurrence of chronic lesions of the pulmonary vessels

3. Cor triloculare biatriatum: the heart consists of two atria and a *single ventricle* with transposition of the great vessels or with their origin in a rudimentary bulbus cordis; *cor triloculare biventriculosum:* there is complete absence of the interatrial septum

4. Persistent AV ostium. a combined partial interatrial and upper interventricular defect

5. Complete transposition of the great arterial vessels

6. Persistent truncus arteriosus: conditions in the cyanotic group, where a *shunt plays no part*, include among others:

(*a*) Pulmonary conus stenosis at the lower bulbar orifice

(*b*) Pulmonary atresia with closed interventricular septum

(*c*) Pulmonary and tricuspid stenosis

nous return to the heart is decreased due to widespread arteriocapillary dilatation and emptying of the venous system. This may result in cessation of the circulation.

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Prevalence and distribution of cardiovascular diseases

LOUIS H. SIGLER

Cardiovascular diseases are the most frequent causes of death and disability. Certain factors such as sex, age, race, and geographic location, which modify the death rates from such diseases, will be discussed in this chapter

CAUSES OF DEATH, CONTINENTAL UNITED STATES

In Table 5-1 and Fig. 5-1 is a summary of the total number of deaths and death rate per 100,000 of the population from all causes, broken up into cardiovascular-renal and other leading diseases in the continental United States in 1950 The cardiovascular-renal group does not include fetal deaths or deaths from syphilis and diabetes, many of which were undoubtedly associated with cardiovascular disease These would add materially to the total number of cardiovascular deaths.

It will be noted from these figures that

TABLE 5-1. DEATHS FROM MAJOR CARDIOVASCULAR-RENAL DISEASES COMPARED WITH OTHER MAJOR CAUSES, CONTINENTAL UNITED STATES, 1950

Major causes	*Total*	*Per* 100,000 *population*	*Per cent of all major causes*
All causes	1,452,454	963 8	100 0
All cardiovascular-renal disease	778,426	516 6	53 6
Cardiovascular disease, all forms	753,749	500 2	51.9
Heart disease, all forms	546,304	362 6	37 6
Rheumatic	22,316	14 8	1 5
Arteriosclerotic	321,003	213 0	22 1
Hypertensive	85,193	56 5	5 9
Congenital malformation	8,675	5.8	0 6
Other forms	109,117	72 4	7 5
Cerebral-vascular disease	156,751	101 0	10 8
[illegible] of heart disease	12,563	8 3	0 9
	30,734	20 4	2 1
	7,397	4 9	0 5
	24,677	16 4	1 7
. .	210,733	139 8	14 6
	81,249	60 6	6 2
	33,959	22 5	2 3
	25,087	16 7	1 7
	64,810	43 0	4 6
Other causes	258,190	164 6	17 0

deaths from cardiovascular-renal diseases comprised 53 6 per cent of deaths from all causes, and deaths from cardiovascular diseases alone, 51.9 per cent If the possible cardiovascular components of fetal deaths and deaths from syphilis and diabetes were taken into consideration, the figure would probably surpass 53 6, even if chronic nephritis and nephrosclerosis were left out, which of course have a pathologic vascular component

It is observed that heart disease alone claimed 546,304 lives in that year, equivalent to 362 6 per 100,000 of the population or 37.6 per cent of all deaths and upward of 72 per cent of the deaths from all cardiovascular-renal diseases. *Arteriosclerotic heart disease* claimed the greatest number of deaths in the heart disease group, comprising 22 1 per cent of deaths from all causes and about 59 per cent of all the deaths from cardiac diseases alone

Hypertensive heart disease was the next most frequent cause of deaths, claiming 85,193 lives, that is, 56 5 per 100,000 population or 5 9 per cent of deaths due to all causes This comprised about 16 per cent of all heart disease deaths.

The combined deaths from arteriosclerotic and hypertensive heart disease was thus about 75 per cent of all cardiac deaths The *other* 25 per cent was distributed among *rheumatic* and other forms of *heart disease*, rheumatic heart disease contributing only about 4 1 per cent.

That and ...
[illegible]

... malignancies The number of deaths from all forms of malignancies in the same year was 210,733 or 139,8 per 100,000 population, which is only 14 6 per cent of all major causes, as compared to 53 6 per cent for the cardiovascular-renal group This is equivalent to only about 27 per cent of the percentage of deaths caused by cardiovascular-renal diseases In other words, for every death from cancer there are about four deaths from cardiovascular-renal diseases.

It is regrettable to find that tuberculosis, infectious and contagious diseases, accidents, suicides and homicides, all of which should theoretically be preventable, still claim many lives However, it is gratifying to find that with modern preventive measures, a comparatively small percentage of deaths is due to such causes In 1950, the combined death rate for all these causes was only 14 8 per 100,000 of the population, which is only 1.5 per cent of all deaths This is a very small percentage compared with deaths caused by cardiovascular-renal diseases

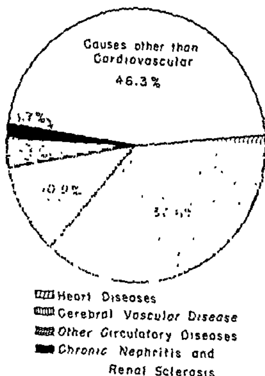


Fig 5-1 Percentages of deaths due to various forms of cardiovascular-renal diseases compared to those caused by all other diseases, United States, 1950.

INFLUENCE OF AGE, SEX, AND RACE

Table 5-2 is an analysis of the death rates from various forms of cardiovascular-renal diseases among males, females, whites and nonwhites, and at different ages. It will be observed that the over-all death rate for all cardiovascular-renal diseases is greater in males than in females, in both the white and nonwhite races Also, the death rate in white males is greater than in nonwhite males. On the other hand, the death rate in nonwhite females is greater than in white females

The various forms of cardiovascular-renal diseases show considerable differences in the death rates in whites and nonwhites, males and females. Thus, the death rates of cerebral vascular disease and hypertensive heart disease are greater in females than in males in both races and are also greater in nonwhite males than in white males. In nonwhite females, it is much greater than in white females, especially in hypertensive heart disease where the

TABLE 5-2 DEATH RATES PER 100,000 POPULATION BY RACE, SEX, AGE, AND TYPE OF MAJOR CARDIOVASCULAR-RENAL DISEASE, CONTINENTAL UNITED STATES, 1950

Cardiovascular-renal disease	*Total*	*White*		*Nonwhite*		*Age*					
		Male	*Female*	*Male*	*Female*	1–4	5–14	15–24	25–44	45–64	65 *and over*
Major cardiovascular-renal diseases	510.8	585 9	439 4	528 4	468 8	3 8	5 5	13 5	75.1	699 1	4,203 7
Diseases of cardiovascular system .	494 4	570 1	425 9	496 3	438 6	2 8	4 6	11 0	68 8	676 4	4,090 3
Cerebral vascular disease	104 0	100 5	103 3	119 5	124 9	0 9	0 5	1 6	11.1	124 6	918 2
Diseases of heart	356 8	434 2	290 6	341 9	283 0	1 6	3 9	8 2	52 9	526 0	2,844 4
Rheumatic heart disease and rheumatic fever	14 8	15 0	14 6	15 3	14 6	0 5	2 9	4 6	11 5	27.9	54 9
Arteriosclerotic heart disease, including coronary .	213 0	294 0	156 0	136 6	91 2	0 1	0 1	1 1	25 5	344 2	1,658 2
Nonrheumatic endocarditis	56 5	59 2	53 9	61 0	51 8	0 3	0 3	0 9	4.5	48 3	553 7
Other diseases of the heart ..	15 9	18 1	11 2	30 3	23 2	0 7	0 5	1 2	4 2	24 4	114 0
Hypertension with heart disease	56 5	47 9	54 8	98 7	102 2	0 0	0 0	0 4	7 2	81 3	463 5
Hypertension without mention of heart disease	8 3	7 8	7 4	14 8	14 6	0 0	0 0	0 2	2 6	10 4	66 2
Generalized arteriosclerosis . .	20 4	21 7	20 9	14 4	11 3			0 0	0 2	6 5	233 5
Other disease of circulatory system	4 9	5 9	3 9	5 7	4 7	0 3	0 2	0 9	2 0	8 9	28 0
Chronic and unspecified nephritis and other renal sclerosis	16 4	15 8	13 5	32 1	30 3	1 0	1 0	2 6	6 3	22 7	113 3

rate for nonwhite females is almost double that of white females For chronic nephritis, the death rates of nonwhite males and females is more than double that of white males and females This is also true for hypertension On the other hand, generalized arteriosclerosis and arteriosclerotic heart disease claim a much greater number of deaths in white than nonwhite males and females, with males greatly predominating in both races.

The *effect of age* on the mortality rates is also very striking. The death rates for all cardiovascular-renal diseases are comparatively low up to 44 years of age. Beyond that there is a sudden increase in mortality for all forms of cardiovascular-renal diseases The greatest rise occurs after 65 years of age.

If we compare the mortality rates from cardiovascular-renal diseases at the various ages among white and nonwhite, males and females, we find marked differences in the various groups, as shown in Table 5-3 The death rates for all ages up to 75 years are much greater in non-whites than in whites, and the reverse is true after that age This means that nonwhites die younger from cardiovascular-renal diseases than do whites It is also noted that the death rates in the younger age groups are higher in white males than females, but in nonwhites the reverse is true.

DEATH RATES IN VARIOUS REGIONS

Table 5-4 is an abbreviated summary of the death rates of major cardiovascular-renal diseases in various parts of the United States in 1950 It will be observed that there are marked

differences in distribution of deaths from these diseases in different regions of the country. The highest death rates appear to be in regions I and II, consisting of states where industry and commerce are the major pursuits and indoor life is most common The lowest death rates are in regions VII and VIII, where agriculture is the predominant pursuit and open-air life is common

Although many regions show fairly uniform death rates in the various states comprising those regions, others show considerable fluctuation in the death rates in the various states, in the same region, as shown in the list on page 5-12 and illustrated in Fig. 5-2.

DEATH RATES IN URBAN AND RURAL AREAS

Figure 5-3 is a graphic representation of the mortality rates, from heart disease alone, in urban and rural areas in the United States and in its subdivisions in 1940 It will be observed that in the majority of States the mortality rates in urban areas were far greater than in rural regions The average death rate from heart disease in the entire country in that year was 338.7 per 100,000 population, with a rural death rate of only 250.6 There are, however, considerable fluctuations in the urban

TABLE 5-3. DEATH RATES PER 100,000 POPULATION FOR MAJOR CARDIOVASCULAR-RENAL DISEASES BY AGE, RACE, AND SEX, CONTINENTAL UNITED STATES, 1950

Age	*White*		*Nonwhite*	
	Male	*Female*	*Male*	*Female*
All ages	585.0	439.4	528.4	468.8
Under 5	5.4	3.9	10.1	8.7
5-14	4.7	5.3	7.9	10.5
15-24	12.2	11.0	26.3	29.6
25-34	31.0	22.0	79.0	89.6
35-44	138.6	65.5	294.1	311.1
45-54	508.1	217.3	902.6	862.5
55-64	1,337.3	664.5	2,115.9	1,933.7
65-74	3,091.8	2,053.3	3,280.4	2,692.8
75-84	7,231.5	6,038.5	5,912.4	4,985.4
85 and over, including unknown	15,969.9	14,564.8	10,842.1	9,327.3

TABLE 5-4 AVERAGE DEATH RATES PER 100,000 POPULATION FOR MAJOR CARDIOVASCULAR-RENAL DISEASES IN VARIOUS REGIONS, CONTINENTAL UNITED STATES, 1950

Region	*Cardio-vascular-renal disease*	*Cardio-vascular diseases*	*Cerebral vascular disease*	*Heart disease*
I	593.6	579.5	113.9	425.3
II	589.7	574.2	97.9	411.0
III	453.2	434.7	99.2	305.8
IV	428.1	406.1	108.9	271.3
V	550.7	534.5	112.7	384.7
VI	546.8	529.3	127.0	362.7
VII	380.7	363.0	82.8	256.2
VIII	415.8	403.5	83.8	290.9
IX	491.3	481.2	97.0	347.0
United States	510.8	491.4	104.0	356.8

Region I. Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont.
Region II Delaware, New Jersey, New York, Pennsylvania.
Region III: District of Columbia, Kentucky, Maryland, North Carolina, Virginia, West Virginia.
Region IV Alabama, Florida, Georgia, Mississippi, South Carolina, Tennessee
Region V: Illinois, Indiana, Michigan, Ohio, Wisconsin
Region VI Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota.
Region VII. Arkansas, Louisiana, New Mexico, Oklahoma, Texas.
Region VIII Colorado, Idaho, Montana, Utah, Wyoming
Region IX Arizona, California, Nevada, Oregon, Washington

and rural death rates in different parts of the country

In some states, as in Arizona for instance, the differences were very marked, the urban death rate having been 374.6 and the rural rate only 136.5 per 100,000 population. In others, as in the East North Central states and in the New England states, the urban and rural rates approximately approach each other, in the Middle Atlantic states, the rural actually surpassed the urban rate.

TRENDS IN MORTALITY

The mortality from cardiovascular-renal diseases has progressively increased since 1900 when the Bureau of Census first began an annual collection of mortality statistics of various

MORTALITY RATES FROM CARDIOVASCULAR-RENAL DISEASE IN VARIOUS STATES, 1950

Region I	
Connecticut	541.4
Maine	603.4
Massachusetts	604.0
New Hampshire	673.4
Rhode Island	586.6
Vermont	620.0
Region II	
Delaware	603.0
New Jersey	576.6
New York	595.7
Pennsylvania	586.7
Region III	
District of Columbia	557.6
Kentucky	472.0
Maryland	524.9
North Carolina	387.9
Virginia	463.6
West Virginia	415.3
Region IV	
Alabama	405.8
Florida	475.3
Georgia	434.0
Mississippi	415.4
South Carolina	414.9
Tennessee	420.0
Region V	
Illinois	599.3
Indiana	574.3
Michigan	470.8
Ohio	548.6
Wisconsin	553.9
Region VI	
Iowa	578.8
Kansas	555.8
Minnesota	510.6
Missouri	600.1
Nebraska	498.7
North Dakota	419.4
South Dakota	453.3
Region VII	
Arkansas	390.1
Louisiana	432.6
New Mexico	238.4
Oklahoma	425.2
Texas	360.0
Region VIII	
Colorado	446.6
Idaho	401.8
Montana	470.2
Utah	346.5
Wyoming	357.3
Region IX	
Arizona	304.3
California	503.2
Nevada	452.9
Oregon	486.2
Washington	503.0

diseases. This increase has been most evident in heart disease. In other circulatory diseases such as cerebral vascular disease, general arteriosclerosis, and hypertension, the increase was relatively small, spotty, and fluctuating. This is shown in Table 5-5.

The marked progressive increase in heart disease during the first half of the twentieth century may partly be apparent, rather than actual Factors that may play a part are better diagnostic acumen on the part of physicians, adoption of clearer certification of causes of death; a progressive increase in the number of states that have contributed to the statistical studies over the years; a greater shift of the population to urban life, and a general increase in longevity due to improved sanitation, the use of antibiotics, and the marked decrease in communicable diseases, resulting in greater aging of the population which contributes most to the deaths from heart disease (Table 5-3). However, allowing for all these possibilities, some of which have been statistically adjusted, there is still an actual increase. This is true especially since 1930, when all states have been contributing to the recordings of mortalities caused by various diseases and since which time other factors mentioned above have been rather stationary

In evaluating the statistical findings in heart disease, it is important to note that, up to 1929, diseases of the coronary arteries were classified under the heading of "diseases of the arteries" Since 1929, following the revision of the International List, coronary artery disease and "angina pectoris" were placed under the sub-

divisions of heart disease. *It is the increase in the prevalence of coronary disease which is greatly responsible for the progressive rise in the mortality from heart disease This increase appears to be actual*

The importance of coronary atherosclerosis and of hypertension as factors in the progressive increase of deaths from heart disease over these years is evidenced by the variation in the mortality rates from heart disease in the various age groups over these years (Fig 5-4). In the younger groups up to about 35 years of age, there has been a progressive decline in the mortality rate from heart disease during the years between 1900 and 1945, reaching almost a straight curve between 35 and 44 years of age Above 45 years, however, there is a steady climb in the mortality rates in the same period. The steady fall in the mortality rates up to 35 years evidently reflects the progressive decrease in the incidence of heart disease due to infections and infectious diseases, particularly rheumatic fever. The steady rise in the mortality rates above 35 years of age is evidently due to progressive increase in the incidence of arteriosclerosis and hypertension, partly associated with increased aging of the population.

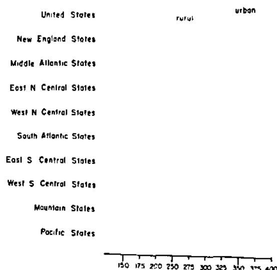


Fig. 5-3. Death rate per 100,000 population in the various geographical subdivisions, United States, 1940, urban and rural districts compared. (*Sigler. Cardiovascular Disease Grune & Stratton. 1949.*)

Seasonal Variability in Mortality. There is considerable seasonal variability in the mortality from all forms of heart diseases. The lowest rates occur in May, June, and July; mortality rises slightly in August and September and more abruptly in October and November. reaching the highest points in December and

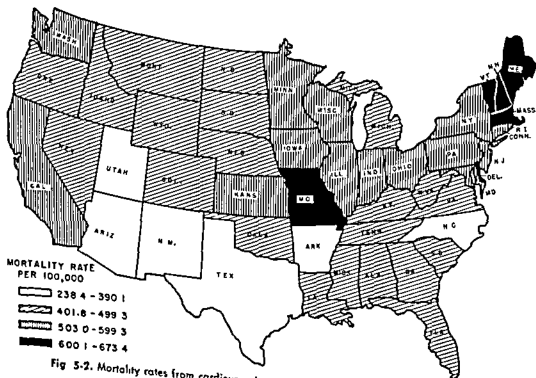


Fig 5-2. Mortality rates from cardiovascular-renal diseases in the various states, 1950.

TABLE 5-5 CRUDE DEATH RATES PER 100,000 POPULATION FOR CARDIOVASCULAR-RENAL DISEASE, REGISTRATION STATES, YEARS 1900–1950

Year	All causes	Heart disease		Cerebral vascular		Arteriosclerosis		High blood pressure		Chronic nephritis	
		No.	%	No.	%	No	%	No.	%	No.	%
1900	1,719 1	137.4	7 9	106 9	6 2			.	..	88 6	5 1
1905	1,588 9	161.9	10 1	105 9	6 0			. .	.	101 2	6 3
1910	1,468 9	158.9	10 8	95 8	6 5			.		94 8	6 3
1915	1,317 6	163 9	12.4	91 5	7 2		.	.		101.5	7.7
1920	1,298 9	159 6	12.2	93 0	7.2			.		88 8	6 8
1925	1,168 1	184 6	15.9	89 5	7 7	..		.	.	95 0	8 1
1930	1,132 1	214 2	18.1	89 0	7 9	18 5	1 6	0 4	0 03	91.0	8 0
1935	1,094 5	245 4	22 4	85 7	7 8	16 9	1 5	0 6	0 05	81.3	7.4
1940	1,074 1	291 9	27 1	90 8	8 5	17 2	1 6	1 0	0 09	81.4	7 6
1945	1,062.1	321 5	30 2	97 9	9 2	19 7	1 9	1 4	0 13	66 7	6 3
1950	963 8	362 6	37 6	101 0	10 8	20 4	2 1	8 3	0 86	16 4	1.7

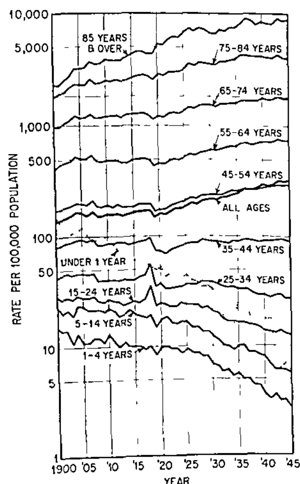


Fig. 5-4. *Age-specific death rates for all forms of heart disease, on logarithmic scale, death registration, United States, 1900 to 1945. (Courtesy of Drs. Woolsey and Moriyama and the Editor of Public Health Reports, Dept of Health, Education and Welfare, P.H.S.)*

January The lowest rate of 6 4 per cent is in July, while the highest of 11.5 per cent is in December There is a somewhat greater seasonal variability in females than in males. Individuals under 20 years of age show the least variability, those over 45, the greatest.

ILLNESS FROM CARDIOVASCULAR-RENAL DISEASES

Our knowledge of the incidence of illness from cardiovascular-renal diseases is comparatively meager because these diseases are not reportable However, some idea of the prevalence of such diseases may be had from a survey made by the U S Public Health Service 1935–1936, with a house-to-house investigation in 83 cities and towns of 18 states. It embraced 700,000 households and a population of 2,500,000 Based on the results of this survey, and calculated on the basis of the 1949 census of population (149,200,000), *it was estimated that, in the United States, about 9,200,000* [illegible] *renal disea*[illegible] *case alone* [illegible] *alone, and 950,000 from chronic nephritis.* With today's census of over 165,000,000 and with the increase in the prevalence of these diseases which has occurred in recent years, *the incidence of cardiovascular diseases should be above 11 million and that of heart disease alone about 6 million* Even these figures are most likely an underestimation of the real facts

because they refer only to diagnosed cases of cardiovascular-renal diseases. There is undoubtedly a great number of cases which are undiagnosed and are not included in the available surveys.

Duration of Illness. Inasmuch as the time of onset of the cardiovascular-renal diseases under investigation naturally varied widely in different individuals, the average duration of illness cannot be definitely determined. In general, however, the average *duration of illness*, from the time it was first diagnosed or the first symptoms appeared to the day of the investigation, was 7.7 years for heart disease, 5.5 years for hypertension, and 6.4 years for nephritis. The average for the entire group was 6.6 years. The distribution of cases according to total duration of illness in years since symptoms were first noticed or the disease was first diagnosed for all investigated cases of cardiovascular-renal diseases was as follows: less than 1 year of illness, 17.8 per cent, 1 to 2 years, 23.0 per cent; 3 to 4 years, 16.3 per cent, 5 to 9 years, 20.5 per cent; 10 to 14 years, 10.5 per cent, 15 to 19 years, 5.6 per cent, and over 20 years 6.4 per cent. All these cases included both disabling and nondisabling cardiovascular-renal diseases.

DISABILITY FROM CARDIOVASCULAR-RENAL DISEASES

Illness from cardiovascular-renal diseases is not always associated with disability. Many individuals can carry on a considerable degree of activity. Others may even carry on normal activity. A good many, however, may have greater or lesser disability for various periods during their lifetime.

Sufficient data are not available as to the exact extent of disability from these diseases.

From an analysis of limited series of cases cited above, we find that the rate of illness from these diseases for both sexes was about 3,769 per 100,000 population. Of these, 418 per 100,000 population (or about 0.4 per cent) required some restriction of activity and 1,838 were totally disabled for 7 days or longer. The entire disability rate was thus 55 per cent. Based on our present census of about 165,000,000 population with an estimated number of 11,000,000 persons suffering from cardio[illegible]
befo[illegible]
wou[illegible]
able [illegible] The economic effect of such an army of disability can be readily appreciated. The rate of disability was found to be greater in females than in males.

In the same series of cases studied, the disability rates fluctuated in different age groups up to about 30 years of age, beyond that there was a steady and progressive rise in disability rate. Thus, under 5 years of age it was 87.2 per 100,000 population, between 5 and 9 years, 121.8; 10 and 14 years, 120.7, 15 to 19 years, 108.0; 20 to 24 years, 148.8, and 25 to 29, 183.6 per 100,000. Beyond 30 years of age, the rise was steady and progressive in each decade, reaching the highest increase at 85 years and over, where the disability rate was 2,811 per 100,000 living population.

An interesting fact brought out in the survey was that the rate of disability had a relationship to the economic status of the patient. Thus, families on relief showed a rate of disability which was 2.7 times greater than that of families with income of $3,000 or more per year, and families with income of less than $1,000 per year showed a disability rate which was 1.6 times greater than that of families with $3,000 or more per year. These differences are probably due to loss of income caused by disease, the hard type of labor in which the poor classes are usually engaged, inability to obtain a less exacting type of work because of lack of training or education, or a combination of these factors.

The duration of disability varied markedly in different individuals. The mean for all cases with disability of 7 days or longer for both sexes and ages was 136 days for heart disease and approximately the same for all cardiovascular-renal diseases. For those cases where disability developed within the year, the mean was 70 days, while in those where disability developed prior to the year, the mean was 295 days.

Confinement to Bed. The mean days spent in bed by disabled cases is naturally less than the mean days of disability. There is no marked difference in this respect between males and females. However, patients below 20 years of age have longer mean days stay in bed than the older age groups. This is undoubtedly due to the fact that most cases of cardiovascular-renal diseases in the younger age groups are rheumatic and require more prolonged bed rest.

The percentage of disabled persons requiring bed treatment for one or more days during 1949 was 84 to 88 per cent for the various forms of cardiovascular-renal disease. With an estimated

6,050,000 cases of disability from these diseases, today it would mean that 5,082,000 to 5,424,000 patients would require such treatment. However, of these, only 20 to 26 per cent were treated in hospitals for one or more days. This would imply that 1,016,400 to 1,410,240 patients with cardiovascular-renal diseases are at present being treated in hospitals one or more days during the year. The average stay in the hospital in that survey was 30 to 34 days in the various cardiovascular-renal diseases where the onset of disability was within the year studied. Where the disability developed prior to the study year, the average stay was 55 to 64 days for the different forms of cardiovascular diseases These figures give an approximate idea of the enormity of the problem and the tremendous expense involved in handling these cases

HEART DISEASE IN CHILDREN AND ADOLESCENTS

As mentioned before, the mortality rates from heart disease in children and adolescents has shown a progressive decrease within the past three decades. This is due mainly to some control of rheumatic fever, which constitutes the major cause of heart disease in early life.

The actual number of cases of heart disease in these age groups in the United States is not definitely known *Recent estimates of the number of cases of rheumatic heart disease alone, in this country, are from one-half million to more than one million.* Such estmates are based on a study of the frequency of occurrence of rheumatic heart disease in various populations of school children in different parts of the country.

In the few reported surveys covering only about 33,827 school children, there was a marked difference in the frequency of its occurrence in different states and even in the same state in different locations. The figures ran between 3 8 and 46 4 per 1,000 children examined.

More information was obtained from a survey of selective service registrants reported from various local boards and induction stations of the armed services in the United States, covering 3,317,441 men. It was found that 10 to 18 per 1,000 registrants were rejected because of the presence of rheumatic heart disease Another survey covering examination of 4,500,000 selective service registrants revealed that *over 300,000 (or about 6 7 per cent) were rejected because of structural or functional heart defects.* The proportion of rejections due to rheumatic heart disease in this series was 28 4 per 1,000, *or 2 84 per cent* This would leave approximately 3 9 per cent of rejections due to other cardiovascular diseases or disturbances.

The incidence of *congenital malformation of the cardiovascular system* is also not definitely known. Judging from the mortality from congenital cardiovascular disease in 1950 (8,675) and assuming that, for every death, there are 15 still alive, the incidence would probably be in the neighborhood of 130,125. This is merely conjectural because many individuals with serious congenital diseases live less than 15 years, while there are mild forms of congenital defects which are not diagnosed. The Crippled Children Program alone has cared for 4,382 cases of congenital cardiovascular disease in 1953

HEART DISEASE IN PREGNANCY

The frequency of heart disease in pregnant women is not great In 76,125 pregnant women in the Boston Lying-in Hospital during a period of twenty-five years, *1,335 or 1.8 per cent had heart disease* Of these, 1,244 or 93.0 per cent had chronic rheumatic heart disease, 69 or 5 2 per cent had congenital heart disease, and 22 or 1 8 per cent had miscellaneous forms of cardiovascular disease such as syphilitic, thyrotoxic, infectious, and others The maternal death rate for the cardiac patients was 3 9 per cent. This death rate, however, had contributed 14 to 28 per cent of all maternal deaths in the various years

In a series of 26,628 pregnancies in the Philadelphia Lying-in Division of the Pennsylvania Hospital, *409 or 1 5 per cent had heart disease.* In this group, 324 or about 79 4 per cent were rheumatic, 51 or 12 5 per cent hypertensive, and 18 or 4 4 per cent congenital The rest had miscellaneous forms, one of which was coronary artery occlusion The functional classification consisted of 206 belonging to Class I, 143 to Class II, 46 to Class III, and 14 to Class IV. Of the entire series of 26,628 cases, 46 patients died, with a maternal mortality from all causes of 0 17 per cent Of these 46 deaths, 14 belonged to the cardiac group, giving a mortality rate of 3 4 per cent. In other words, *cardiac disease contributed 20 per cent of all maternal deaths in this series*

Reports from other large medical centers show about the same incidences of cardiac disease in pregnant women, with a great predominance of the rheumatic group. It is thus seen that, although the incidence of heart disease in pregnancy is not great, it is an important factor in increasing the mortality rate.

DETECTION OF EARLY CARDIOVASCULAR DISEASES

An important method of discovering early cardiovascular diseases would be screening of the general population. To date, very little has been done in that respect. The examination of selective service registrants, mentioned before, helped discover many unsuspected cases of heart disease and yielded considerable knowledge of the incidence of heart disease in the general population

Recently, attempts have been made in a few large cities to screen the general population for cardiovascular diseases The methods employed in some areas were the use of roentgenologic and electrocardiographic examinations In other areas more complete examinations were made, including history taking, auscultation, and blood pressure determinations in addition to roentgenologic and electrocardiographic studies. Of 27,724 presumably normal individuals so screened, 4,783 or a little over 17 per cent have been found to have actual or suspicious cardiovascular disease. More careful reexamination of these 4,783 showed that only 1,997, or upward of 7 per cent of the 27,724 original cases, actually had some form of cardiovascular disease

Another source of uncovering the presence of cardiovascular diseases in the general population is the x-ray surveys widely conducted in recent years for the detection of tuberculosis In 1953, over 15 million chest x-rays were taken throughout the country. Suspected presence of cardiac disease was found in 0.1 to 1 0 per cent in different parts of the country

CARDIOVASCULAR DISEASES IN THE WORLD

The incidence and prevalence of cardiovascular diseases in parts of the world other than in the United States appear to be less known than in this country Some idea, however, may be had from reported mortalities This is shown, for many countries, in Table 5-6 which gives the total deaths from all causes with the death rate per 100,000 population, the total deaths from cardiovascular diseases with their death rates, as well as the percentage of cardiovascular deaths in relation to deaths due to all other causes.

It is observed that *England, Wales, Northern Ireland, Scotland, Australia,* and *New Zealand* have the highest death rates and percentages of deaths from cardiovascular diseases. The figures nearly approach those of the United States. Next in death rates and in the percentages of deaths from such disease are *Sweden, Switzerland, Denmark, Finland, the Republic of Ireland, and Canada* Austria shows a similarly high cardiovascular death rate, but the percentages of deaths in relation to deaths due to other causes is smaller. This is due to a much greater general death rate there *France, West Germany, Belgium, Norway, Italy,* and *Spain* have lower death rates as well as lower percentages of deaths from cardiovascular diseases. *The Netherlands, Portugal, Yugoslavia,* and *Israel* are next lower in rates and percentages. Still lower are *Argentina* and *Japan.* The lowest in rates and in percentages of deaths from cardiovascular diseases are *Chile, China (Taiwan), Mexico, Egypt,* and *the Philippines.* It is interesting to observe that in *Taiwan* and *the Philippines,* with low mortality rates and percentages from cardiovascular diseases, the general mortality rates from other causes is likewise relatively low. On the other hand, in *Chile, Mexico,* and especially in *Egypt,* the general mortality rates are extremely high. This is particularly true in Egypt, where the general mortality rate in 1952 reached a figure of 2,024 3 per 100,000 population, which is the highest rate of all countries. This would indicate that the majority of the population here die from various other diseases and only relatively few die from cardiovascular diseases. Inasmuch as most of the cardiovascular diseases are degenerative and develop beyond adulthood, it means that most of the death in such countries occur in the early years of life before such diseases set in This is evidenced by the fact that the mortality rate from arteriosclerotic heart disease in Egypt is very low, as shown in Table 5-6

It will also be observed from Table 5-7 that arteriosclerotic heart disease and cerebral vascular disease contribute most of the deaths from cardiovascular diseases In nearly all countries, however, arteriosclerotic heart disease is a more frequent cause of death than cerebral vascular disease. The exceptions are Portugal, Mexico, Japan, and Chile, where the

TABLE 5-6. NUMBER OF DEATHS AND DEATH RATES PER 100,000 POPULATION FROM ALL CAUSES AND FROM CARDIOVASCULAR DISEASE IN FOREIGN COUNTRIES IN THE GIVEN YEAR

Country	*Total deaths*			*Deaths from cardiovascular disease*		*Per cent of cardiovascular deaths*
	Year	*Number*	*Rate*	*Number*	*Rate*	
France	1954	512,726	1,192.4	152,067	353.7	29.6
West Germany	1953	539,134	1,100.7	175,903	359.1	32.6
Austria	1954	84,632	1,214.5	31,133	446.8	36.7
Belgium	1953	105,863	1,206.0	32,202	366.9	30.4
Denmark	1954	39,885	905.3	17,259	391.7	43.2
Finland	1953	39,925	964.1	16,056	387.7	40.2
Netherlands	1953	80,551	767.7	29,428	280.5	36.5
Norway	1953	28,412	845.8	10,962	326.2	38.5
Sweden	1953	69,553	969.9	30,850	430.2	44.3
Switzerland	1953	49,684	1,018 7	20,610	422.6	41.4
Italy	1953	476,015	1,003.4	175,949	370.9	36.9
Spain	1950	300,989	1,080 1	93,397	331.6	30.7
Portugal	1954	95,088	1,093.8	25,215	290 0	26.5
Yugoslavia	1953	30,845	825 2	8,576	229.5	27.8
England and Wales	1953	503,529	1,141.6	235,295	533.4	46.7
North Ireland	1954	15,124	1,090 2	7,355	530 2	48 6
Scotland	1954	61,380	1,198.0	30,785	600.9	50.1
Republic of Ireland	1953	34,591	1,174 6	13,910	472.3	40.2
Egypt	1952	181,031	2,024 3	8,452	94.4	4.6
Israel	1954	9,635	642 1	3,405	226.9	35.3
Canada	1954	124,520	820 9	56,001	369 2	44.9
Mexico	1952	408,823	1,498 4	26,168	95 9	6.4
Argentina	1952	152,360	844 6	37,832	209.7	24.8
Chile	1953	80,068	1,263 7	12,399	195.6	15 4
Philippines	1952	175,952	852 2	5,464	26.5	3.1
Japan	1953	772,547	891 1	182,171	210.2	23.5
Australia	1953	80,188	909 6	38,431	435 9	47.9
New Zealand	1953	17,009	884 4	8,552	444 8	50.2
China (Taiwan)	1953	78,078	945 1	8 827	106 8	11.3

death rates from cerebral vascular disease are greater than from arteriosclerotic heart disease. Of these, however, only *Japan* definitely has a greater cerebrovascular death rate The other three countries have a very high death rate classed as "other heart diseases," most of which might have been arteriosclerotic heart disease which was misdiagnosed

Although arteriosclerotic heart disease is the most prevalent form of cardiovascular disease and far surpasses in death rates its next competitor cerebral vascular disease, the relative frequencies of these two diseases vary greatly in the various countries In some countries, such as *England, Wales, Northern Ireland, Scotland, the Republic of Ireland, Australia,* and *New Zealand*, the mortality rates from both diseases are very high, although that of cerebral vascular disease is much lower. On the other hand, in *France, West Germany,* and *Austria*, the death rates from cerebral vascular disease, although lower than those of arteriosclerotic heart disease, is rather high in relation to the incidence of heart disease. In fact, in *West Germany*, the death rate from cerebral arteriosclerosis, which is 155 9 per 100,000 population, closely approaches that of arteriosclerotic heart disease, which is only 163 3 per 100,000 population In *Switzerland, Sweden, Canada, Denmark,* and *Finland*, the death rates from cerebral arteriosclerosis is intermediary in relation to arteriosclerotic heart disease between the two groups of countries mentioned above. In *Belgium, the Netherlands, Norway, Italy, Yugoslavia, Israel,* and *Portugal*, the death rates from arteriosclerotic heart disease is relatively

smaller. The lowest of the European group is *Portugal*, with a death rate from this disease of only 67 1 per 100,000 However, it is questionable if this actually represents the real mortality rate A high death rate of 71 1 per 100,000 here is classified under "other heart diseases," many cases of which might have been misdiagnosed arteriosclerotic heart disease.

The mortality rates from hypertension and *hypertensive heart disease* in the various countries are far lower but generally have a fairly parallel relationship to the mortality rates from arteriosclerotic heart disease. Those countries which have a high death rate from arteriosclerotic heart disease also have a fairly high death rate from hypertension This is not true of all countries.

The death rates from rheumatic heart disease vary greatly in the different countries. It appears to be highest in *Italy, England, Wales*, and in *Taiwan* In the last, it appears to be the outstanding cause of death from cardiovascular disease In *West Germany*, it is lowest, contributing only 1.3 deaths per 100,000 population

CONCLUSIONS

From the limited statistical findings presented here, certain theoretical considerations may be proposed as to etiology of the cardiovascular diseases and some suggestions offered as to their possible control.

The extremely high death rates from these diseases, especially from arteriosclerotic heart disease, in the United States and in all other English-speaking countries in widely separated areas of the world, suggest that the ethnic origin of these peoples may play some part in the pathogenesis of these diseases Although all

TABLE 5-7. DEATH RATES PER 100,000 POPULATION FROM DIFFERENT FORMS OF CARDIOVASCULAR DISEASE IN FOREIGN COUNTRIES

Country	*Rheumatic heart disease*	*Arteriosclerotic heart disease*	*Hypertensive heart disease*	*Hypertension, no mention of heart disease*	*Cerebral vascular disease*	*Other heart diseases*
France		209.6		4.7	140.4	
West Germany	1.3	163.3	11.4	3.0	155.9	24.2
Austria	17.9	195.2	8.8	6.2	159.1	59.6
Belgium	7.5	111.8	18.0	28.7	59.6	141.3
Denmark	7.2	202.2	21.4	3.8	121.9	35.2
Finland	6.7	191.7	36.5	2.7	119.3	30.8
Netherlands	5.6	147.3	10.1	4.7	94.4	18.4
Norway	9.4	135.3	20.7	5.2	123.5	32.1
Sweden	5.9	229.5	20.8	3.6	135.2	35.2
Switzerland	9.2	238.1	18.8	5.9	130.7	19.9
Italy	20.1	176.3	24.8	6.4	130.5	13.6
Spain	Not specified		52.5		90.4	188.7
Portugal	16.4	67.1	13.5	9.7	112.2	71.1
Yugoslavia	17.8	124.6	2.8	1.3	64.2	18.8
England and Wales	20.0	293.0	25.6	18.4	154.3	17.1
Northern Ireland	10.6	288.7	30.0	12.1	150.4	38.4
Scotland	16.8	336.8	20.8	16.3	186.6	23.6
Republic of Ireland	12.1	274.8	17.2	10.0	110.9	40.7
Egypt	14.6	28.2	2.1	24.2	11.7	13.6
Israel	12.0	120.9	4.2	7.0	69.1	13.7
Canada	10.4	222.9	26.7	6.4	90.5	12.3
Mexico	5.0	5.5	0.2	2.1	16.2	66.0
Argentina	Not specified		15.6		60.5	134.2
Chile	4.8	36.2	11.0	5.1	47.7	99.8
Philippines	Not specified		12.6		7.3	6.6
Japan	4.2	44.7	1.5	9.3	134.2	16.3
Australia	8.8	240.9	26.3	14.9	121.1	23.9
New Zealand	11.4	252.2	29.1	7.5	117.1	27.5
China	19.2	3.7	0.9		53.2	30.8

TABLE 5-6 NUMBER OF DEATHS AND DEATH RATES PER 100,000 POPULATION FROM ALL CAUSES AND FROM CARDIOVASCULAR DISEASE IN FOREIGN COUNTRIES IN THE GIVEN YEAR

Country	*Total deaths*			*Deaths from cardiovascular disease*		*Per cent of cardiovascular deaths*
	Year	*Number*	*Rate*	*Number*	*Rate*	
France....	1954	512,726	1,192.4	152,067	353.7	29.6
West Germany	1953	539,134	1,100.7	175,903	359.1	32.6
Austria..	1954	84,632	1,214.5	31,133	446.8	36.7
Belgium...	1953	105,863	1,206.0	32,202	366.9	30.4
Denmark	1954	39,885	905.3	17,259	391.7	43.2
Finland	1953	39,925	964.1	16,056	387.7	40 2
Netherlands	1953	80,551	767.7	29,428	280.5	36.5
Norway	1953	28,412	845.8	10,962	326.2	38.5
Sweden	1953	69,553	969 9	30,850	430.2	44.3
Switzerland	1953	49,684	1.018.7	20,610	422.6	41.4
Italy	1953	476,015	1.003 4	175,919	370 9	36.9
Spain	1950	300,989	1,080 1	93,397	331 6	30 7
Portugal	1954	95,088	1,093.8	25,215	290.0	26.5
Yugoslavia.	1953	30,845	825.2	8,576	229.5	27.8
England and Wales	1953	503,529	1.141 6	235,295	533.4	46.7
North Ireland	1954	15,124	1,090 2	7,355	530.2	48.6
Scotland.	1954	61,380	1,198.0	30,785	600.9	50.1
Republic of Ireland	1953	34,591	1,174 6	13,910	472.3	40.2
Egypt	1952	181,031	2,024 3	8,452	94.4	4.6
Israel	1954	9,635	642.1	3,405	226.9	35.3
Canada	1954	124,520	820 9	56,001	369 2	44.9
Mexico	1952	408,823	1,498 4	26,168	95.9	6.4
Argentina	1952	152,360	844 6	37,832	209.7	24.8
Chile	1953	80,068	1,263 7	12,309	195.6	15.4
Philippines	1952	175,952	852 2	5,464	26 5	3 1
Japan	1953	772,547	891 1	182,171	210.2	23.5
Australia	1953	80,188	909 6	38,431	435 9	47.9
New Zealand	1953	17,009	884 4	8 552	441 8	50.2
China (Taiwan)	1953	78,078	945 1	8,827	106.8	11.3

death rates from cerebral vascular disease are greater than from arteriosclerotic heart disease. Of these, however, only *Japan* definitely has a greater cerebrovascular death rate. The other three countries have a very high death rate classed as "other heart diseases," most of which might have been arteriosclerotic heart disease which was misdiagnosed.

Although arteriosclerotic heart disease is the most prevalent form of cardiovascular disease and far surpasses in death rates its next competitor cerebral vascular disease, the relative frequencies of these two diseases vary greatly [illegible]. In some countries, such [illegible] *Scotland*, [illegible] and *New* *the Republic of* [illegible] *Zealand*, the mortality rates from both diseases are very high, although that of cerebral vascular disease is much lower. On the other hand, in *France*, *West Germany*, and *Austria*, the death rates from cerebral vascular disease, although lower than those of arteriosclerotic heart disease, is rather high in relation to the incidence of heart disease. In fact, in *West Germany*, the death rate from cerebral arteriosclerosis, which is 155.9 per 100,000 population, closely approaches that of arteriosclerotic heart disease, which is only 163 3 per 100,000 population. In *Switzerland*, *Sweden*, *Canada*, *Denmark*, and *Finland*, the death rates from cerebral arteriosclerosis is intermediary in relation to arteriosclerotic heart disease between the two groups of countries mentioned above. In *Belgium*, *the Netherlands*, *Norway*, *Italy*, *Yugoslavia*, *Israel*, and *Portugal*, the death rates from arteriosclerotic heart disease is relatively

problem There is no denying that the laboratory must play a great role in our study of these diseases, but we believe that a greater role must be played by broader studies on a statistical basis

For immediate control of these diseases, an attempt must be made to discover their incipiency in the individual case, for guidance This is to be done by widespread screening of the population We feel that this can be best accomplished by the general practitioner who is to be made conscious of the problem and is to be taught to recognize the early phases of these diseases This means that more time must be devoted to teaching the art of clinical diagnosis and the recognition of these diseases. Unfortunately this art has of late begun to lose ground in the profession, partly because the maze of modern laboratory experimentation may seem to make clinical observation superfluous.

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3

Cardiovascular disease in the Orient

MARIANO M. ALIMURUNG

In recent years, the study of cardiovascular epidemiology has gained importance as a source of vital data, not only for the purpose of knowing the importance and distribution of heart disease in different parts of the world but also for the discovery of certain clues that may furnish important information of etiologic significance.

Paul D. White, in 1940, said.

> Heart disease is a world problem, as much as is tuberculosis or dysentery or influenza, but it has not yet been investigated as such, in contrast to many of the infectious diseases which have ravaged the world, especially in the form of waves
>
> . . . . .
>
> leaving for us of the present day the study and control of the less dramatic, more insidious and gradual, but no less fatal maladies, such as heart disease and cancer. International cooperation and world-wide study have become the matter of fact procedure in dealing with the serious infections The pioneer work of the Rockefeller Foundation and other groups transcending national boundaries has broken the ground and shown the way It should not then be too hard to follow their footsteps in the collection of invaluable information about the most important causes of heart disease and the incidence and severity of their effect on the heart under all sorts of conditions and in every corner of the globe. Nature has for centuries been conducting gigantic experiments as to the effects of climate, of type of work, of diet, and of local or world-wide diseases on men, women, and children of different races, that are spread out before our very eyes for us to record and to analyze, quite readily yielding information that might never be obtainable by our own experiments on man

Twelve years later, following a visit to several Oriental countries including Pakistan and India, Dr White found the confirmation to his earlier statement. He remarked,

> Heart disease, without any doubt, is one of the most serious, perhaps the most threatening malady of our times, not only in the Western world but also in the East . . . Contrary to old ideas, rheumatic heart disease, hypertension, and coronary heart disease were common in those countries even though their true prevalence has been somewhat masked by the high incidence in the past of infectious disease and faulty nutrition

In 1954 this world-wide impact of heart disease became more clearly demonstrated as statistical reports of the incidence of heart disease from different countries were submitted at the Second World Congress of Cardiology. Data from Oriental countries, particularly from the Far East, have been comparatively scarce in the literature Further, there has been the erroneous impression that heart disease, at least in some of its types, does not constitute an important problem in the Orient Hence, a proper appreciation of this important chapter of cardiovascular epidemiology is necessary, if any conclusion is to be derived from comparative analyses with data from other parts of the world

Papers on the incidence and importance of cardiovascular diseases have appeared in Indian journals The inaccessibility of these publications to most workers the world over has not made possible an adequate appreciation of the above data In the Philippines, studies have so far been limited to surveys in the large general hospitals of Manila. In Japan, the survey is still

going on, and only fragmentary information is available.

HEART DISEASE IN INDIA

Vakil (1954) presented data on heart disease in India on the basis of a 5-year study (1941–1945) during which he reviewed 30,104 patients that were admitted to the medical wards of a hospital in Bombay. The majority of the patients were from the "low-income groups," mostly laborers, mill hands, and domestic servants

In this survey, Vakil found 1,860 cases with ... of 6.0 per

dence was observed in the fifth decade of life, 24.3 per cent of the total number of cardiac patients

Table 5-8 shows the percentage distribution of the various etiologic forms of heart disease in Vakil's series. It is seen that the leading etiologic types were the *hypertensive* and *coronary*, 33 4 per cent together, and the *rheumatic*, 24 7 per cent If, however, the hypertensive were separated from the coronary cases, then rheumatic heart disease assumes the leading figure.

Of additional interest in this study were the apparent differences in the occurrence of heart disease among four large racial groups studied Hindus, Moslems, Christians, and Parsees and Jews First of all, Vakil observed a relatively higher incidence of heart disease among Christians, Parsees and Jews than among the Hindus In the second place, he pointed out racial differences in the various etiologic types. This is

TABLE 5-8. PERCENTAGE INCIDENCE OF THE VARIOUS ETIOLOGIC TYPES OF HEART DISEASE IN INDIA

Etiologic type	*Per cent of total*
Hypertensive and coronary	33.4
Rheumatic	24 7
Miscellaneous	11 3
Syphilitic	12 9
Pulmonary	10 0
Unknown	5.6
Bacterial	1 1
Congenital	1.0

seen in Table 5-9. Thus, whereas syphilitic heart disease is more frequent among Moslems, the hypertensive and coronary types seem more preponderant among the Christians and the group of Parsees and Jews.

Contrary to a number of previously reported studies on the low incidence of *rheumatic heart disease* in the tropics, Vakil's data gave support to other more recent reports showing the high incidence of this disease in various parts of Bengal, United Provinces, Punjab, Madras, Ceylon, and Bombay. In Vakil's series, there was no noticeable difference in the incidence of rheumatic heart disease between the white races and the dark races. The disease apparently was more frequent during the hotter months of the year, and there was a predomi-

... incidence was 12 9 per cent Among those with this type of heart disease, 56 3 per cent were Moslems and only 27.9 and 12.9 per cent were Hindus and Christians, respectively. Of interest is the finding that 27 6 per cent of these patients developed aortic aneurysms;

TABLE 5-9 PERCENTAGE DISTRIBUTION OF RACIAL GROUPS IN THE VARIOUS ETIOLOGIC TYPES OF HEART DISEASE IN INDIA

Group studied	*No cases*	*Moslem*	*Hindu*	*Christian*	*Others*
Congenital	19	89.4	10 6	0	0
Rheumatic	461	71.1	17.2	8 7	3.0
Syphilitic	240	56.3	27.9	12 9	2.9
Hypertensive and coronary	768	50 6	15.2	23.4	10.8
Pulmonary	185	75 3	12.4	9.1	3.2
Bacterial	20	75 0	15 0	5.0	5.0
Miscellaneous and unknown	315	60.4	16.8	12.6	4.2
All heart cases	1,860	62.3	17.2	14.8	5.7
All medical cases	30,104	70.2	14 9	12 2	2.7

these occurred 7.7 times more frequently in the thoracic aorta than in the abdominal aorta.

Vakil's report that 29 per cent of his cardiac patients had *hypertensive heart disease* was a higher rate of occurrence than previously reported in other Indian series As it would be expected, 92.9 per cent of them were labeled essential hypertension. The highest incidence was observed in the fifth and sixth decades of life, accounting for 55 per cent of the cases. Only 6.4 per cent of them were below 30 years of age.

Coronary heart disease, 13.5 per cent of the cardiac patients, showed the highest incidence (35.6 per cent) in the fifth decade of life Apparently coronary heart disease in India involves the Christians, Parsees and Jews more often than the Moslems. Vakil found 16.4 per cent of these patients below 40 years of age, 6 of whom were under 30.

Chronic cor pulmonale appears to be a prominent cardiac problem in India. In this survey, Vakil reported 10 per cent of his cardiac patients with this type of heart disease, 64 4 per cent being between 40 and 59 years of age. Asthma, emphysema, and chronic bronchitis were either singly or jointly responsible for 69 4 per cent of these cases. Padmavati reported similar findings in New Delhi (1956).

HEART DISEASE IN THE PHILIPPINES

The first postwar report on heart disease in the Philippines was made by Alimurung and Grajo, based on the case records of a large hospital of Manila. Subsequently, a more extensive study was done in conjunction with three other large hospitals in Manila. This study was based on 67,826 case records from the medical and pediatric service. Since one hospital series accounts for a preponderantly male population because it originates in an army hospital, the remaining data from the other three hospitals, totaling 53,662 case records, were analyzed as one composite group As in the series of Vakil in India, this Philippine survey was on patients in the charity wards and, therefore, belonged to the low-economic group.

In this series, there were 4,304 cardiac patients, 8 per cent of the total. Of interest is the fact that this was an average derived from a consistently increasing yearly occurrence from 6 8 per cent in 1947 to 10 1 per cent in 1953. As a cause of death, heart disease was responsible for 716 deaths This represented 14 1 per cent of all deaths and 16 6 per cent of admissions for heart disease.

Figure 5-5 shows the relative frequencies of the various etiologic types of heart disease in

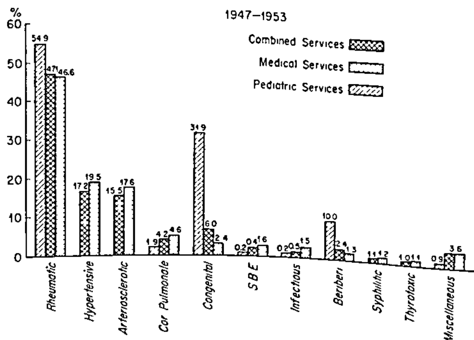


Fig. 5-5. Relative frequency of different etiologic types of heart disease in the Santo Tomas University Hospital, Philippine General Hospital, and North General Hospital (in the Philippines).

this Philippine survey In both the medical and pediatric services, rheumatic heart disease was the leading cause, accounting for 46 6 per cent in the *medical group*, 54 9 per cent in the pediatric group, and 47.1 per cent in the combined series Such a high rate of occurrence of rheumatic heart disease was attributed to the frequency of streptococcic infections. further enhanced by the setback in living conditions following World War II.

Hypertension, *arteriosclerosis* (*coronary* heart disease), and *cor pulmonale* figured next in the adult cardiac patients, whereas congenital cardiac malformations were second among the children

As in India, *chronic cor pulmonale* appears to be a relatively prominent type of heart disease in the Philippines In the present series, 4.2 per cent of the patients had this condition In a subsequent study covering a 9-year period (1947 to 1955), Torralba and Abmurung analyzed cases of cor pulmonale seen in a teaching hospital and found a relative incidence of 8 6 per cent among all cardiac patients Of these, 59 (75 per cent) were between the fourth and sixth decades of life There were four pediatric patients, the youngest being 1 year and 7 months old The leading types of pulmonary disease in these patients were bronchial asthma and pulmonary tuberculosis. 57 and 25 per cent, respectively.

When compared with three other series from Mexico, New England, and Texas, the data obtained in the Philippines showed some interesting differences (1) a similar frequency of occurrence of rheumatic heart disease with that of Mexico (41 per cent) and much lower than *that of the* United States, (2) a higher rate of chronic cor pulmonale than *any of these* three Western series, (3) a remarkably lower rate of syphilitic heart disease, and (4) impressive rates for hypertension and coronary heart disease, probably higher than previously suspected

HEART DISEASE IN JAPAN

The spectrum of heart disease in Japan is currently being surveyed (*Maekawa*) The revealing study of Kimura on 10,000 *postmortem* examinations at a *teaching* hospital *is most* impressive, however This extensive *study* disclosed only 73 cases with myocardial infarction, a distinctly low figure. Kimura went further and personally examined 1,007 hearts in order to study more closely coronary arteriosclerosis. He found that the incidence *of severe coronary arteriosclerosis in Japan is about one-tenth of that in persons of the same age in the United States.*

In searching for possible factors relating to the development of coronary sclerosis, Kimura *observed the* following: (1) among the males, there was no difference on the basis of the place of lifelong residence, (2) *among the females*, the disease occurred more frequently among city women than among country women; (3) the incidence was 20 to 50 per cent higher among the men who used alcohol and tobacco; and (4) there *appeared* no *significant* difference based on the type of work done, whether physical or mental.

From the point of view of vital statistics, Kusukawa *reviewed data* from 1935 to 1951 and reported an increase in the death rate from coronary heart disease over these 16 years, being 7.5 per 100,000 in 1935 and slightly less than 10 per cent in 1951. Myocardial disease likewise rose from 11 to 13 deaths per 100,000, *then* increased abruptly to 21 per cent in 1947, 25 in 1949, and 36 in 1951 In general, the data showed a similar pattern of increasing frequency. Kusukawa attributes this trend *to* either an absolute increase in frequency of *heart disease* or an increasing accuracy of diagnosis of heart disease in more recent years The particularly interesting observation is the fact that the prevalence of coronary disease remains at a low level

SUMMARY

The three sources of data on heart disease in the Orient—India, Philippines, and Japan—reveal that heart disease is also an important problem in *these* countries Moreover, there seems to be an increasing *number of* cardiac patients due to either an actual increase of heart disease or an increasing accuracy in diagnosis.

Rheumatic heart disease appears as the most frequent single etiologic type.

Chronic cor pulmonale seems *to be* a comparatively important problem in the Orient. Bronchial asthma and pulmonary tuberculosis appear to be the main pulmonary diseases responsible for this cardiac condition.

Coronary heart disease has a strikingly low incidence in Japan. In India and the Philippines, this disease has not yet attained the high rate of occurrence in the United States, but it does account for approximately 15 per cent of all heart cases.

Hypertensive heart disease is also gaining ground, ranking second among the types of heart disease seen.

Syphilitic heart disease is vanishing in the Philippines, although it still occurs quite frequently in India, especially among the Moslems.

Although responsible for only 1 per cent in India, congenital cardiac malformations were seen in 6 per cent of cardiac patients in the Philippines. This is probably due to greater accuracy of diagnosis and not to an actual greater incidence.

These data prove beyond doubt that heart disease is a truly universal problem Epidemiologic studies are therefore needed, particularly because they may yield information of great value in the search for those clues that would offer solution to many unsolved aspects of heart disease.

4

Mechanisms of certain symptoms and signs in cardiovascular disease

Jaundice, Ascites, Cyanosis, Clubbing, Peripheral Edema, Dyspnea
BLAS MOIA

Gallop Rhythm; Alternans
ALDO A. LUISADA

JAUNDICE

In spite of the marked circulatory and parenchymatous alterations of the liver in prolonged congestive failure, jaundice is not frequent in [illegible]

jaundice when present is not marked, as these patients usually have a certain amount of *cyanosis*, the combination of both gives a characteristic yellowish-bluish color to the skin [illegible]

en [illegible]

the [illegible]

would support Ottenberg's hypothesis that the slight amount of bilirubin in the fluid of edema is due to the *small* percentage of proteins of this fluid, which cannot absorb much pigment. On the contrary, the ascitic fluid has a high concentration of protein

Hyperbilirubinemia in heart failure can be due to three basic mechanisms biliary regurgitation, hepatic insufficiency, *and* increased production of bilirubin *Levels of both direct* and indirect bilirubin can be found elevated, even though the alkaline phosphatase level is generally within normal limits or *slightly elevated* (Sherlock). It is evident that *the increase* in amount of direct bilirubin in the blood is due to a certain degree of obstruction or biliary *regurgitation*. This finding has been explained as the *result of a compression* of the biliary capillaries by the dilated venules, brought *about by the marked venous hypertension or obstruction* by biliary thrombi (Eppinger), and *also a disruption of the biliary capillaries produced by centrolobular hemorrhagic necrosis* (*Lopez García et al*). Cardiac catheterization and needle biopsy of the liver disclosed a *relationship between the severity* of this anatomic *alteration* and the increased pressure in the hepatic veins (Giraud et al).

This biliary regurgitation must *play an important role* in the production of jaundice in cardiac failure, but certain authors discount its value (Sherlock)

Another important cause is the inability of the hepatic cells to absorb and excrete blood bilirubin The remarkable *alterations of the hepatic* parenchyma explain the altered hepatic function. As shown by biopsy, these alterations may range from simple changes in the cells surrounding the *centrolobular* veins to actual necrosis in areas that extend *more than* one-third of the *radius* of the lobule, possibly followed by *cirrhosis* (*Sherlock*) Alteration may be present without *evident* histologic changes, as a result of the *oxygen deficiency caused* by

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It is evident that as water and sodium stagnate in the abdominal cavity, the body tends to retain them, and that such retention facilitates an increase of ascitic fluid, resulting in a vicious circle. Finally, the hypoproteinemia due to constant shift of proteins into the abdominal cavity will aggravate the condition.

Although the ascitic fluid accumulated in the peritoneal cavity appears as a steady deposit, there is actually a dynamic equilibrium with the blood (Hyatt et al.) According to McKee et al., there is a complete turnover of the albumin of the ascitic fluid in about 2 days; according to Prentice et al, from 40 to 80 per cent of the total ascitic fluid is removed and replaced each hour[1]

Ascites caused by *constrictive pericarditis* disappears after pericardiectomy, this clearly confirms the important role played by venous hypertension in its production It is well known that prolonged cardiac failure causes liver cirrhosis The permanent constriction of the intrahepatic veins due to chronic congestion can determine an irreversible ascites, even though the pressure of the inferior vena cava is diminished

It is evident that all factors that favor edema in congestive failure will aggravate existing ascites

CYANOSIS

Cyanosis occurs when the capillary blood has more than 5 Gm/100 ml of reduced hemoglobin (Lundsgaard et al) Each gram of hemoglobin fixes 1.33 vol oxygen. Therefore, normal blood *containing 15 Gm hemoglobin* per cent should fix 20 vol of oxygen In normal human beings, the blood is not completely oxygenated in the lungs, so that it usually has about 95 per cent saturation. This could be described also by saying that if the blood leaves the lungs saturated with 19 vol oxygen, it has 5 per cent degree of unsaturation and 0 75 Gm/100 ml of reduced hemoglobin

In passing through the tissues, the blood loses normally about 5 vol oxygen, so that the venous blood has 6 vol oxygen *less than the completely saturated blood* It has consequently a 30 per cent degree of unsaturation and 4 5 Gm/100 ml of reduced hemoglobin

[illegible]

It has been calculated that the quantity of hemoglobin of the capillary blood is equal to one-half the sum of the quantity of reduced hemoglobin in the arterial blood plus that of the venous blood. Consequently, in the last example, it will be

$$\frac{0\,75 + 4\,5}{2} = 2\,6 \quad \text{Gm/100 ml}$$

It is easy to notice that in order to obtain 5 Gm/100 ml reduced hemoglobin in the capillary blood, the quantity of reduced hemoglobin in the arterial blood is the most important element. Let us assume that the blood leaves the lungs saturated only by 75 per cent, i e , that it lacks 5 vol oxygen in order to be completely saturated and has 3.75 Gm/100 ml reduced hemoglobin It will lose, as usual, 5 vol oxygen in passing through the tissues, so that the venous blood will have a drop of 10 vol oxygen from the original level and has consequently 7 5 Gm/100 ml reduced hemoglobin. The capillary blood will have, then, $(3.75 + 7.5)/2 \approx 5\,62$ Gm/100 ml reduced hemoglobin, i e., enough to produce cyanosis.

Let us suppose instead that the blood leaves the lungs with a normal saturation (95 *per cent*) but, in its course through the tissues, loses 10 vol oxygen per cent instead of 5, then, it will have 7.5 Gm/100 ml reduced hemoglobin, and the capillary blood will have $(0\,75 + 7\,5)/2 = 4.12$ Gm/100 ml reduced hemoglobin, or not enough to cause clinical cyanosis.

Unsaturation of the arterial blood may be due to altered blood circulation of the lungs or its mixture with venous blood through a shunt Cyanosis occurring because of this mechanism is called *central cyanosis.*

Unsaturation of the venous blood is seen in slowing of the *peripheral* circulation (so-called "stasis") like that caused by heart failure (congestive failure). Cyanosis of this type is called *peripheral cyanosis.* It occurs only in advanced heart failure with marked decrease of cardiac output and very slow peripheral circulation. This mechanism, however, often increases the cyanosis caused through another mechanism. Any factor that *tends* to accelerate local circulation (local warmth, massage, etc.) leads to local disappearance of the peripheral cyanosis [illegible]

[illegible] cause of cyanosis is the mixture of poorly oxygenated (venous) blood with normally oxygenated (*arterial*) blood through anomalous shunts *of the* heart or vessels. This type of "central cyanosis" is characterized by

the disturbed hepatic circulation or the poor saturation of blood in the lungs (Keefer et al.; Rich et al.). It has been proved that in chronic cardiac failure, splanchnic blood flow may be decreased by as much as 33 per cent, so that the venous hepatic blood is even more unsaturated. It is possible that the oxygen tension of the blood is not sufficient to maintain alive all the cells while the blood flows from the periphery to the interior of the lobule.

Hepatic failure is accentuated if blood leaves the vessels (pulmonary infarct, severe and lasting pulmonary stasis) and there is an increase in production of bilirubin that must be excreted by the liver (Keefer et al.; Rich et al.). Although a different mechanism is involved, bilirubin can also be retained as a consequence of a marked decrease of cardiac output, then hepatic blood flow and consequently the amount of bilirubin offered to the hepatic cell to be excreted decrease and bilirubin is retained in the blood An intramuscular injection of blood (the same amount as is destroyed in a pulmonary infarction) does not produce hyperbilirubinemia in patients with cardiac failure. Therefore, Rich and Resnik believe that the mechanism by which pulmonary infarction produces or aggravates jaundice is not the increased amount of bilirubin but a decreased oxygen saturation of the blood in the lungs In addition, it is evident that pulmonary embolism produces a marked aggravation of cardiac failure, which further impairs liver function Whatever the mechanism, it is clear that pulmonary infarction is not indispensable for the causation of jaundice. Consequently, with or without pulmonary infarction, jaundice in cardiac failure depends upon the structural lesions that facilitate biliary regurgitation and the functional impairment of the hepatic cells. For this reason, it is only observed in severe and lasting cardiac failure.

Certain drugs, such as chlorpromazine (Morritt et al.), methyltestosterone, etc., when administered to these patients, can also produce jaundice.

ASCITES

Ascites is the transudation of fluid into the peritoneal cavity It has the same meaning as hydrothorax, hydropericardium, and peripheral edema. It appears in the advanced state of right heart failure. However, certain aspects of ascites justify a discussion of its mechanism.

In constrictive pericarditis and tricuspid insufficiency, ascites may appear very early and last for a long time, even though peripheral edema is not severe. Besides, while edema fluid contains not more than 0.5 per cent of proteins, the ascitic fluid usually contains from 2 to 3 per cent. Exudates obviously would contain a higher percentage.

Ascites may be favored or caused by various factors, such as increase of portal pressure, decrease of colloid osmotic pressure of the serum, disturbance of the lymphatic circulation due to intrahepatic venous hypertension, excess of antidiuretic hormone, and disturbances of the electrolytic metabolism (Snell). However, the increased pressure of the hepatic veins has probably the greatest importance Experimental portal hypertension usually does not cause ascites and is a stimulus to the establishment of collateral circulation. However, in man, portal obstruction due to extrahepatic alterations is at times accompanied by ascites, especially when the collateral circulation is not well developed (Baggenstoss et al).

Ascites usually does not appear after ligation of the inferior vena cava, if this is made below the hepatic veins; on the contrary, it appears constantly if the ligation is made above the opening of these veins or if the hepatic veins are ligated (McKee et al.; Volmiller et al). Several authors (Koback) have produced experimental ascites by this procedure. Milnes has observed that in such conditions, the ligature of the portal vein does not improve the ascites and that, on the contrary, the latter decreases spontaneously (Volwiler et al) or following ligation of the hepatic and splenic arteries (Berman et al.). In human beings, *the wedge pressure of the hepatic veins, which seems to be similar with portal venous pressure,* was found raised in patients with cirrhosis of Laennec, especially in the presence of esophageal varicosities and jaundice, but was not related to the presence or absence of ascites (Taylor et al).

Consequently, as suggested by Child, most of the ascitic fluid transudes from the hepatic surface and is primarily due to intrahepatic venous hypertension, which increases lymphatic flow according to hydrodynamic laws (Starling) The high concentration of albumin in the ascitic fluid is explained by the fact that the capillaries of the liver are extremely permeable to proteins (Starling).

It is evident that as water and sodium stagnate in the abdominal cavity, the body tends to retain them, and that such retention facilitates an increase of ascitic fluid, resulting in a vicious circle. Finally, the hypoproteinemia due to constant shift of proteins into the abdominal cavity will aggravate the condition.

Although the ascitic fluid accumulated in the peritoneal cavity appears as a steady deposit, there is actually a dynamic equilibrium with the blood (Hyatt et al.). According to McKee et al., there is a complete turnover of the albumin of the ascitic fluid in about 2 days; according to Prentice et al., from 40 to 80 per cent of the total ascitic fluid is removed and replaced each hour.[1]

Ascites caused by *constrictive pericarditis* disappears after pericardiectomy, this clearly confirms the important role played by venous hypertension in its production. It is well known that prolonged cardiac failure causes liver cirrhosis. The permanent constriction of the intrahepatic veins due to chronic congestion can determine an irreversible ascites, even though the pressure of the inferior vena cava is diminished.

It is evident that all factors that favor edema in congestive failure will aggravate existing ascites.

CYANOSIS

Cyanosis occurs when the capillary blood has *more than 5 Gm/100* ml of reduced hemoglobin (Lundsgaard et al.). Each gram of hemoglobin fixes 1.33 vol oxygen. Therefore, normal blood containing 15 Gm hemoglobin per cent should fix 20 vol of oxygen. In normal human beings, the blood is not completely oxygenated in the lungs, so that it usually has about 95 per cent saturation. This could be described also by saying that if the blood leaves the lungs saturated with 19 vol oxygen, it has 5 per cent degree of unsaturation and 0.75 Gm/100 ml of reduced hemoglobin.

In passing through the tissues, the blood loses normally about 5 vol oxygen, *so that the venous blood has 6 vol oxygen less than the* ...

... of reduced hemoglobin.

[1] This is conf... toneal injec... idly as an ... Editor.

It has been calculated that the quantity of hemoglobin of the capillary blood is equal to one-half the sum of the quantity of reduced hemoglobin in the arterial blood plus that of the venous blood. Consequently, in the last example, it will be

$$\frac{0.75 + 4.5}{2} = 2.6 \quad \text{Gm/100 ml}$$

It is easy to notice that in order to obtain 5 Gm/100 ml reduced hemoglobin in the capillary blood, the quantity of reduced hemoglobin in the arterial blood is the most important element. Let us assume that the blood leaves the lungs saturated only by 75 per cent, i.e., that it lacks 5 vol oxygen in order to be completely saturated and has 3.75 Gm/100 ml reduced hemoglobin. It will lose, as usual, 5 vol oxygen in passing through the tissues, so that the venous blood will have a drop of 10 vol oxygen from the original level and has consequently 7.5 Gm/100 ml reduced hemoglobin. The capillary blood will have, then, $(3.75 + 7.5)/2 = 5.62$ Gm/100 ml reduced hemoglobin, i.e., enough to produce cyanosis.

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Unsaturation of the venous blood is seen in ... Cyanosis of this type is called *peripheral cyanosis*. It occurs only in advanced heart failure with marked decrease of cardiac *output* and very slow peripheral circulation. *This mechanism*, however, often increases the cyanosis *caused* through another mechanism. Any factor that tends to accelerate local circu*lation* (local warmth, massage, etc.) leads to local disappearance of the *peripheral* cyanosis while it does not change central cyanosis.

In *congenital malformations of the heart*, the fundamental cause of cyanosis is the mixture of poorly oxygenated (venous) blood with normally oxygenated (arterial) blood through anomalous shunts of the heart or vessels. This type of "central cyanosis" is characterized by

the disturbed hepatic circulation or the poor saturation of blood in the lungs (Keefer et al; Rich et al.). It has been proved that in chronic cardiac failure, splanchnic blood flow may be decreased by as much as 33 per cent, so that the venous hepatic blood is even more unsaturated. It is possible that the oxygen tension of the blood is not sufficient to maintain alive all the cells while the blood flows from the periphery to the interior of the lobule.

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The widening and deformation of the distal portions of the fingers and toes are fundamentally due to *increased volume and thickness of the soft tissues*, accompanied by changes in the nails ("glass watch nails"), which sometimes become a prominent feature. The skin of these parts is unusually warm

In general, hypertrophy of the phalanges is observed only in advanced clubbing and does not contribute to this process In children, the growing of the soft tissues can be of such magnitude as to determine an atrophy of the phalanx through compression (Weens et al.).

The hyperemia and edema of these areas explain why clubbing may occasionally appear *in acute form* (McCord et al) and may also disappear, if its cause is removed A typical example is observed in bacterial endocarditis: as soon as the antibiotic treatment is able to *control the infection*, one can observe a groove that clearly limits the curved distal part of the nail from the normally growing proximal part

The ossifying periosteal lesions are usually seen early and with predominance in the distal parts of the radius, cubitus, tibia, and fibula. They have a tendency to progress toward the proximal portion of these bones but do not usually involve the joints (Gall et al.). *In the most* advanced cases, the metacarpal and *metatarsal* bones (rarely the phalanges) *may become involved* (Gall et al.). In some cases, lesions of the *scapula*, patella, iliac crest, nose, or zygomatic process have been observed (Kessel et al; Paterson). Although this process is usually bilateral and symmetrical, it may predominate in *one or the* other section

The periosteal inflammation is characterized by *infiltration of* lymphocytes and plasma cells. It produces a "pseudocortex," with the formation of a new subperiosteal bone *that finally* becomes united with the *original* bone cortex and thickens it (Gall et al.).

The joints may present chronic synovitis and degenerative changes *of the* cartilage, which are not specific for clubbing *This* explains why patients sometimes *complain* of pain in the limbs (Gall et al.).

The above changes are *commonly* observed in various cardiac and pulmonary diseases, especially *in those* that are accompanied by cyanosis. They *may* also be found in diseases of other *systems* (pyelonephritis, ulcerative colitis, bacillary *dysentery*, regional enteritis, sprue, biliary cirrhosis, chronic intoxications, etc.) (Carr; Locke, Mendlowitz).

There also is a *congenital form of clubbing*, which appears with familial character in healthy persons. This type of alteration is easily recognized because it is not accompanied by periosteal inflammation and because the soft tissues on the sides of the nails maintain their normal form

The mechanism responsible for clubbing and its associated lesions is still controversial (Mendlowitz). In most cases, *the change could* be due to increased blood *flow in the limbs*, but *this does not apply to the* congenital form *An increase of* blood flow may be caused in part by a higher digital arterial pressure. In a case of pulmonary abscess, the remission of clubbing coincided with the *normalization* of flow and digital arterial pressure due to *surgical* removal of the abscess In other *chronic inflammatory processes, not* accompanied by clubbing, the digital blood flow *seems to be normal* (Mendlowitz).

The fact that when clubbing is associated *with* hypertrophic osteopathy, digital circulation is not increased, might be interpreted as being due to a stabilization of the phenomenon in the fingertips while increased blood flow *still* occurs in the bones (Mendlowitz).

In cyanotic congenital heart diseases, *the* severe dilatation *of the capillaries* and venules, with the *corresponding* stasis of blood rich in *hemoglobin and red* cells, might be a possible factor (Redisch et al.).

The toxic, infectious factor may be responsible for clubbing in certain cases (e.g., *in* bacterial endocarditis—when the infection is treated, *clubbing* disappears). However, there *is probably* an indirect connection, because many other chronic infections *do not* cause clubbing. The possible *intervention* of neurogenic (Locke) or endocrine *factors (Fried)* has been advocated. *It* would be logical to admit that when *certain infectious* or degenerative processes are localized in certain organs or tissues, they produce substances which, through an unknown mechanism, accelerate blood flow *in* the fingertips and thus originate clubbing

The hypoxic blood would act *in* the same way, as in congenital *malformations* of the heart, respiratory diseases with *alveolar* hypoventilation, etc. *According to Levy et al*, clubbing is *always* connected with *anoxemia*. Mauer

decreased oxygen saturation of the arterial blood while that of the pulmonary veins is normal. It is obvious that the mixture occurs after the entrance of the pulmonary blood in the left atrium.

When there is a functional cause of poor oxygen intake in the lungs (low pressure of the atmosphere—high altitude) or an organic cause (pulmonary disease), the blood cannot be properly oxygenated during its passage through the pulmonary capillaries. A similar disturbance occurs in a pulmonary arteriovenous fistula which permits a bypass of the capillaries of the lungs (Moia et al). In all these cases, there is another type of *central cyanosis,* in which both the arterial blood and that of the pulmonary veins present a low oxygen saturation.

When there is either a functional or an organic disturbance of the oxygen intake in the lungs, inhalation of 100 per cent oxygen decreases the cyanosis. This test has been suggested as a simple method for differentiating central cyanosis caused by pulmonary diseases from central cyanosis caused by right-to-left shunt. However, cyanosis may decrease somewhat also in the latter cases (Montgomery et al), although very slowly (Gullickson et al). The change is due not to a pulmonary factor of anoxemia but to the fact that during inhalation of pure oxygen, this gas dissolves in plasma (up to 2 vol/100 ml) (Selzer), thus contributing to the oxygenation of reduced hemoglobin in the venous blood.

The diminution of pulmonary flow, as observed in severe pulmonic stenosis, probably also plays a role in causing cyanosis of certain congenital malformations of the heart (Taussig and Blalock).

Even though anastomosis of one peripheral artery with a branch of the pulmonary artery, proposed by Blalock and Taussig in order to increase this inadequate pulmonary circulation, markedly improves cyanosis in certain congenital malformations of the heart, the mechanism causing the change is still under debate. In fact, *isolated pulmonary stenosis does not cause cyanosis.* When there is cyanosis, it is due to the concomitant existence of a right-to-left shunt.

Selzer points out that in a similar case, there was, before surgery, a 2-liter shunt and a 2-liter flow through the lungs After the operation, pulmonary flow was increased from 2 to 4 liters and consequently the systemic flow was increased from 4 to 6 liters. As 2 liters of the increased systemic flow went from the systemic to the pulmonary system, the venous return to the right ventricle would not be changed but pulmonary flow would be twice as large as before. The 2 liters of venous blood that were shunted were mixed with 4 liters of arterial blood instead of with 2 liters, and the percentage of concentration of the reduced hemoglobin was proportionally decreased This explains the disappearance or attenuation of the cyanosis

As a result, the Blalock-Taussig operation is not a specific treatment for either Fallot's tetralogy or pulmonic stenosis. All conditions in which venous and arterial blood are mixed before entering the systemic circulation can benefit by it, because the proportion of oxygenated blood is increased. Cyanosis improves not because of an increased amount of oxyhemoglobin but because of a decreased concentration of reduced hemoglobin. It is necessary to keep in mind that *cyanosis is related not to the greater or lesser quantity of oxyhemoglobin but to the absolute concentration of reduced hemoglobin and, therefore, is not dependent upon the relationship between reduced hemoglobin and oxyhemoglobin* (Lundsgaard).

If the quantity of hemoglobin contained in the blood is decreased, there will be less reduced hemoglobin, and vice versa This is why it is more difficult to find cyanosis in anemic patients, on the contrary, cyanosis is much more readily found in polycythemic patients In polycythemia vera," which is not secondary to arterial [illegible] the percentage of oxygen saturation (and [illegible] the venous and systemic blood) is normal but the absolute value of reduced hemoglobin can be increased over the threshold of cyanosis simply as a consequence of the unusual increase in number of red blood cells (Selzer)

Finally one should remember that often both central and peripheral mechanisms act together and, in certain conditions, are modified by peripheral factors, such as the number and size of capillaries and the thickness and pigmentation of the skin

CLUBBING

Clubbing of fingers and toes is characterized by a rounded, thick appearance of the distal phalanges. *Periostitis,* mainly of the long bones, is frequently associated with it, and there may be joint symptoms (Gall et al.).

nisms. In hyponatremia (not therapeutically induced), water is retained, although the concentration of sodium is lower than normal. In spite of this, more sodium than water seems to be retained. This demonstrates that a certain *amount of sodium* is preserved in body reservoirs (bones, cartilages, *connective* tissue) (Mokotoff et al.; Talso et al.), or possibly within the cells.

The fact that in some endocrine conditions, either spontaneous or artificially induced by corticosteroids, sodium retention and edema are observed, led to the theory that renal retention of sodium in cardiac failure is mediated *through hormonal* factors. Certain authors have found a greater elimination of glucocorticoids (Parrish) and especially of aldosterone (Axelrad et al.; Davis et al., Pechet et al.). The same finding has been obtained in experimental animals (Davis et al.). However, this increase in the urinary excretion of aldosterone has not been confirmed by others (Driscol et al.; Muller et al.). The observation that the urinary elimination of aldosterone in dogs after ligation of the inferior vena cava gradually rises while, at the same time, ascites is present, led to the belief that the increased secretion of aldosterone is not necessary to initiate water and sodium retention, and that its greater elimination is the result, not the cause, of this retention.

The most interesting point is that in normal dogs (Davis et al.) or dogs with bilateral *adrenalectomy* (Gaudino et al.), the administration of large *doses* of DCA produces only a transitory retention of sodium. *On the contrary*, there is an almost complete *retention of sodium*, accompanied by formation *of ascites*, when DCA is administered to *adrenalectomized* dogs after the ligature of *the inferior* vena *cava* (*Davis* et al.). *Besides, in* normal persons, in whom the intake of *sodium* was reduced to 11 mEq daily, greater elimination of aldosterone was found. It is evid*ent that the* edema of experimental cardiac failure cannot be produced if there is no adrenal activity. It is possible that in the edematous state, there is no adrenal hypersecretion but simply a difficulty in the *hormonal* destruction, caused by the functional impairment of the liver (Laragh et al.).

The retention of sodium *precipitates* a greater secretion of *pituitary antidiuretic hormone*, and this increases the reabsorpt*ion of* water *in the* distal tubules and water retention. Consequently, this is a factor that intervenes only in a second, late stage. Hyponatremia observed spontaneously in patients with severe congestive failure suggests that, in certain conditions, antidiuretic hormone production is independent of osmoreceptor control (Hanenson et al.).

A final summarization of the numerous studies leads to the conclusion that in the genesis of edema of cardiac failure, *the initial and fundamental* factor is the increase of hydrostatic pressure, causing the plasma to filter water and sodium in the interstitial spaces. A homeostatic mechanism starts acting and leads to retention of sodium in order to compensate for the loss.

DYSPNEA

Every *normal* person has "consciousness of the necessity *to increase* the respiratory effort" (Meakins) *during* severe physical exertion, especially *if he* has had no adequate training. This dyspnea may have a mechanism similar to that observed in cardiac failure. However, the latter has certain characteristic aspects: (1) it appears with physical effort or emotional states that *previously* did not produce respiratory *difficulty*; (2) it lasts longer than usual after *the cause* is removed, and (3) it impairs the *functional* capacity of the patient, preventing him *from accomplishing* an effort that was within his *ability prior* to the onset of failure.

That an abundant *diuresis* produced by mercurials is followed by a rapid relief *of* dyspnea proves that pulmonary venous engorgement plays an important role in the genesis of dyspnea.

Whether because of left *ventricular* failure or mechanical block (*as in* mitral stenosis), blood accumulates in the *lungs*, and the circulation becomes slower but occurs under greater *pressure in the pulmonary venous and* capillary systems. *Loss of compliance* of the lungs occurs, *probably* with compression of the alveoli, *and interstitial* and alveolar edema may occur.

The marked diminution of vital capacity, tidal volume, and *inspiratory* and expiratory *reserve* is then *easily explained*. Compensatory *tachypnea increases* the respiratory minute volume, but the *maximal* respiratory capacity is decreased because *hyperpnea* is obtained through an increase *in* respiratory rate, not [illegible] h of respiration.

believes that even in the absence of arterial unsaturation, clubbing may occur if there are accelerated sedimentation rate of the red cells and a wide vascular bed that favors the formation of intravascular *rouleaux;* the latter interfere with tissue oxygenation by a decrease of the diffusion surface per unit of hemoglobin.

PERIPHERAL EDEMA

Edema of heart failure has been classically explained as one of the results of venous hypertension. The increase in hydrostatic pressure of the venous-capillary bed favors filtration of water and electrolytes in the intercellular spaces. The small amount of protein content of the edema fluid (0.2 to 0.5 per cent) (Stead et al.) shows that usually there is no increase of capillary permeability.

Many data confirm the importance of *venous hypertension* as the basic cause of edema. In venous obstruction (caused by compression, surgical ligation, following phlebitis, etc.), *localized edema* is produced. In clinical or experimental hypoproteinemia, with or without renal lesions, edema is present because a "relative increase" of hydrostatic pressure is caused by the decrease of colloid osmotic pressure of the plasma.

Ligation of the inferior vena cava causes ascites if it is located above the hepatic veins, but not if it is placed between the latter and the renal veins. In acute left ventricular failure, pulmonary edema occurs.

The importance of the increased hydrostatic pressure in the genesis of edema has been, however, discussed or denied by some authors (Goldman et al., Warren et al.) because the same degree of venous hypertension may or may not be associated with edema in different clinical cases. Moreover, after disappearance of failure, the administration of sodium increases edema without an increase of venous pressure (Goldman et al., Warren et al.). When digitalis is discontinued in patients in failure on salt-poor diet, venous pressure may rise without increase of weight (Newman et al.; Reichsman et al.).

In general, this and other observations show that in spite of increased venous pressure, edema will not occur or will appear with difficulty if the body does not have abundant material to develop it. Besides, it is evident that exercise, hypoproteinemia, tissue pressure, etc., are secondary factors that may contribute to the appearance and distribution of the edema of cardiac failure.

The hypothesis that increased venous pressure in cardiac failure is not a direct consequence of failure but *is due to the increased blood volume,* caused by sodium and water retention, plus the effect of *reflex venoconstriction,* cannot be accepted without reservation.

The fact that severe experimental lesion of the right ventricle does not produce venous hypertension (Starr et al.) is not a decisive proof, because in this condition, venous return to the left ventricle is also severely decreased. With an extracorporeal pump maintaining left ventricular output in a dog, in which acute right ventricular failure had been produced, venous pressure becomes a linear function of left ventricular output. On the contrary, this does not happen when the right ventricle works normally. This confirms that right ventricular failure is the direct cause of the increase in venous pressure and circulating blood volume (Rose et al.).

Several investigators claim that edema in cardiac failure is due to diminution of renal excretion of sodium, followed by water retention. According to this theory, venous hypertension is a secondary phenomenon and would determine only the appearance and localization of the edema. The hypothesis that this decrease of renal excretion of sodium is caused by a diminution of glomerular filtration as a result of reduced renal blood flow is, for many reasons, untenable.

Instead, there are numerous proofs that in cardiac failure there is an increase in tubular reabsorption of sodium. If water and sodium are exuded from the plasma to the intercellular spaces, a homeostatic mechanism tends to retain water and sodium in the body in order to compensate for the loss. It should be kept in mind that in cardiac failure, the amount of interstitial fluid becomes greater than the total amount of plasma (Friedberg). At the same level of elevated hydrostatic pressure, edema increases when a patient's diet contains too much sodium and decreases when sodium is restricted or is eliminated by means of diuretics.

Water retention appears to be fundamentally secondary to sodium retention, since it is necessary to maintain the isotonic state.[2] However, water can be retained through other mecha-

[2] See also Part 18, Chap. 4. *Editor.*

duces real relief is the vertical (thus the name *orthopnea*). In the supine decubitus, pulmonary congestion increases as a result of increased cardiac output and venous return. It is also possible that in the supine position, the sensitivity of the respiratory center is increased as a consequence of these circulatory changes or other unknown mechanisms; in some patients, elevation of the head by means of one or two pillows is sufficient to give relief, though some orthopnea still persists (Harrison).

In severe and protracted dyspnea at rest, expiratory wheezes and musical rales can be heard, simulating those of bronchial asthma. Spirograms are also similar in both conditions. Both *bronchospasm* and *bronchial edema* play a role in causing this type of respiration and aggravate dyspnea, as demonstrated by the fast relief that follows the administration of aminophylline, ACTH, or prednisone

Paroxysmal dyspnea and *acute pulmonary edema* have a similar pathogenesis and must be considered as the most severe degree of cardiac dyspnea Evidently they are due to a sudden occurrence or intensification of pulmonary congestion[3] Whatever the factors of congestion, it is evident that this is the basic cause of the paroxysmal attacks, as demonstrated by the relief obtained through the orthopneic position and the beneficial effect of venesection. However, it is not easy to explain why the attacks appear predominantly at night and paroxysmally Increased venous return caused by the supine position, and possibly by sleep (Halmagyi et al), is probably one factor. To this should be added at times an increase of circulating plasma due to hemodilution, favored by the recumbent position (Perera et al).

It is likely that during sleep, the respiratory center has a lower sensitivity and does not react proportionally to the increase of centripetal impulses determined by the pulmonary congestion. As soon as the patient awakes, as a result of this condition or for any other cause, the center recovers its sensitivity and reacts with intense hyperpnea.

When the increase of pulmonary congestion is severe and sudden, especially if the patient has not developed an increase of the pulmonary arteriolar resistance, the hydrostatic pressure of the pulmonary capillaries becomes higher than the threshold of 25 to 35 mm Hg, and transudation of fluid occurs. This fluid accumulates in the alveoli, interalveolar spaces, and bronchial walls beyond the capacity of reabsorption of the pulmonary lymphatic vessels (Drinker et al.).

Dyspnea in Neurocirculatory Asthenia.[4] Patients without cardiac failure, with or without organic cardiac disease, may have tachypnea and dyspnea of effort, or even at rest, besides the other characteristic manifestations of functional cardiovascular disease (Friedman). These patients have a tendency to use the diaphragm only slightly during normal respiration and to breathe chiefly with the intercostal and accessory muscles. The time of apnea after a period of forced hyperventilation does not increase significantly with respect to the one registered before the test; this is characteristic of this condition (Friedman).

This type of dyspnea is associated more frequently than is generally realized to the dyspnea of cardiac failure, and, in some cases, may aggravate or precipitate attacks of paroxysmal dyspnea because tachypnea facilitates venous return to the right heart, thus increasing pulmonary congestion.

Cheyne-Stokes Respiration. The periodic respiration of Cheyne-Stokes is due to diminished *stimulation* of the respiratory center, in the presence of either normal sensitivity with *hypocapnia* (as in high altitudes or during forced hyperventilation) or, more commonly, decreased *sensitivity* with normal concentration of carbon dioxide in the blood. Both factors often occur simultaneously.

When the stimulation of the respiratory center is decreased, a period of apnea is produced, usually in an expiratory position (Wassermann). The interruption of pulmonary ventilation causes the accumulation of carbon dioxide in the arterial blood (*hypercapnia*) and *hypoxia* When hypercapnia and hypoxia reach the maximum, the respiratory center is intensely stimulated, both directly and through stimuli acting on the chemoreceptors Then a phase of hyperpnea supervenes, in which the retained carbon dioxide is eliminated, anoxia is corrected, and the patient returns to the apneic period.

The fundamental factor that causes and perpetuates periodic respiration is not the lack of

[3] See Part 18, Chaps 10 to 14 for details pertaining to pulmonary edema. *Editor.*

[4] See also Part 17, Chap. 2 *Editor.*

Hepatomegaly, abdominal distention, ascites, and pleural or pericardial effusion, when present, increase intrapleural pressure and aggravate the effects of pulmonary congestion.

In spite of these changes, there is no alteration of blood oxygenation, except in advanced cases or those with pulmonary complications.

The following facts demonstrate that the different types of dyspnea in cardiac failure result from pulmonary congestion, not from alterations of the respiratory center or changes of blood chemistry.

1. Neither diminution of cerebral blood flow (Moyer et al.; Novak et al.) nor increase in the arteriovenous difference of oxygen between carotid and internal jugular bloods (Cullen et al.) has been demonstrated. Moreover, there are conditions (such as shock) in which cardiac output is diminished but dyspnea does not occur.

2. Oxygen saturation of the arterial blood is normal in patients with dyspnea (Meakins, Novak et al.) or is only slightly subnormal (Platts), at rest as well as after moderate exercise (Cullen et al.). Only in severe cardiac failure, cardiac failure with pulmonary complications, or after extreme effort, does one find low levels of oxygen saturation that can stimulate the chemoreceptors (Ruskin). Patients with congenital malformation of the heart and severe oxygen arterial unsaturation may not have dyspnea. This demonstrates that the diminution of oxygen in the venous blood has no importance as a factor of excitation of the peripheral respiratory chemoreceptors (Aviado et al.). However, a moderate diminution of oxygen arterial saturation might contribute to stimulation of the respiratory center if this is already abnormally stimulated by other impulses.

3. Dyspnea cannot be attributed to an increase in carbon dioxide of the arterial blood, first, because carbon dioxide is easily eliminated by hyperventilation, and, second, because of its greater diffusion from the alveolar walls. Therefore, except when there are severe pulmonary complications, the amount of carbon dioxide in the arterial blood, alveolar air, and exhaled air may even be lower than normal (Harrison).

4. This behavior of carbon dioxide explains the eventual occurrence of alkalosis (Fraser et al.) in left ventricular failure with dyspnea. On the other hand, when there is pulmonary involvement with hypoventilation, *hypercapnia* may occur, followed by acidosis. In severe and advanced cardiac failure following renal insufficiency or due to ammonium chloride, or after severe exercise, acidosis may appear. It is then due to accumulation of lactic and pyruvic acids and will increase the severity of the dyspnea. This type of dyspnea, however, tends to lose its superficial character and assumes that of deep hyperventilation, as seen in diabetic acidosis (Friedberg).

Mechanism by Which Pulmonary Congestion Originates Dyspnea. The decreased compliance of the lungs and the decreased distention of the alveoli increase the discharge of centripetal impulses that stimulate vagal terminations and originate tachypnea (Harrison). It is possible that the distention of pulmonary vessels (Aviado et al.) contributes to produce or exaggerate tachypnea by a reflex vagal mechanism (Churchill-Cope).

The various factors have more or less importance according to the different types of dyspnea. In *exertional dyspnea,* pulmonary reflexes are elicited by the pulmonary congestion, which is the result of a markedly increased cardiac output, and have great importance. Muscular contraction or passive muscular movements may produce hyperventilation; the latter disappears after nerve section (Harrison). The author does not believe that these reflexes are the basic cause of dyspnea in patients with cardiac disease, because the dyspnea increases progressively and is then transformed into dyspnea at rest. Besides, in any of these conditions, the therapeutic decrease of pulmonary congestion lessens dyspnea. It is probable that during intensive effort, secretion of hormones (epinephrine), accumulation of acids (lactic acid) and other metabolites, as well as hypoxia and hyperthermia may all be contributory factors.

In *dyspnea at rest,* pulmonary congestion is greater and is followed by the various mechanical and reflex changes that have already been discussed. This type of dyspnea increases in the supine position; this is a useful sign in differentiating it from other types of dyspnea.

The patient usually avoids left lateral decubitus because it produces more dyspnea (*trepopnea*) (Wood et al.). This is possibly because of gravitational shift of the enlarged heart, diminution of venous pulmonary drainage, and increase of pulmonary inflow with decrease of vital capacity (Ruskin). The position that pro-

systolic AV pressures occurred in some cases during atrial relaxation, suggesting the possibility of a valvular mechanism occasionally involved in the production of the late component of the atrial sound

In regard to the 3d sound, in the past, a *triple rhythm* (gallop) was considered as a purely auditory phenomenon However, phonocardiography has revealed that in certain persons with a triple rhythm, a diastolic sound is rather large but is inaudible because it is weak, low-pitched, or too near the 1st sound.

The author, together with Rottman, tried to separate the cases with a more "physiologic" triple rhythm from those with a more "pathologic" triple rhythm. It was decided to classify as "more pathologic" any case having a diastolic sound with the following graphic characteristics: (1) frequency of vibrations of 30 or more per second, irrespective of its amplitude; (2) amplitude greater than two-thirds of the loudest of the two main sounds at the apex; or (3) both This empirical classification has no absolute value because the "pathologic" is merely the *accentuation of a "physiologic" phenomenon*, and the pitch of the pathologic sound may be similar to that of the normal sound. More recently, Friedland and Jacono studied the triple rhythms by means of filters (Part 3, Chap. 9). The conclusion was that, in some pathologic cases, the frequency of the vibrations of the extra sounds is the same as that of the normal extra sounds (3d and 4th sounds).

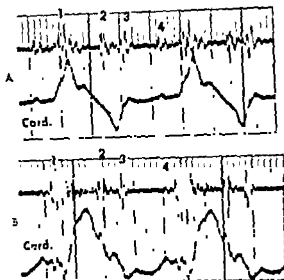


Fig 5-7. A. Hypertensive and coronary heart disease. Stethoscopic and linear tracings at apex. Quadruple rhythm due to large 3d and 4th sounds. B. Hypertensive and coronary heart disease. Stethoscopic and linear tracings at apex. *Triple rhythm* due to large 3d sound in early diastole.

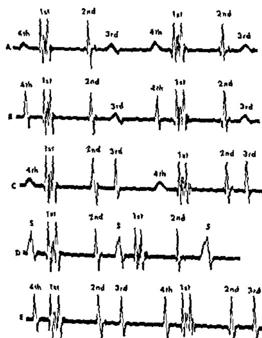


Fig 5-6. Scheme of triple and quadruple rhythms. A. Normal B. Triple rhythm (large 4th sound). C. Triple rhythm (large 3d sound). D Triple rhythm (summation type). E. Quadruple rhythm (large 3d and 4th sounds). (From Luisada. Heart Beat. Hoeber, New York, 1953)

Phonocardiagram, Low-frequency Tracings. Three types of triple rhythm have been recognized (Wolferth and Margolies, Braun-Menéndez) (Fig 5-6).

1. *Atrial type.* The additional sound occurs at the time of atrial contraction and represents the accentuation of the 4th sound (Fig. 5-8A). It usually falls *in late diastole*, but if the P–R interval is long and diastole is short, it may fall in mid-diastole or even early diastole.

2. *Ventricular type.* The additional sound falls *in early diastole*, at the time of rapid filling, and represents the accentuation of the 3d sound. It occurs from 0.14 to 0.18 sec after the 2d sound in adults (Fig. 5-7B).

3 *Summation (or "nondescript") type.* There is an additional sound or a short, rumbling murmur in mid-diastole. This is due to the more or less simultaneous occurrence, first, of rapid passive filling, and then of atrial contraction, causing the rapid succession, or fu-

oxygen but the diminished reactivity of the respiratory center to carbon dioxide. For this reason, inhalation of oxygen prolongs the periods of apnea (Harrison, Uhlenbruck) while inhalation of carbon dioxide regularizes respiration The oxygen saturation has been found normal in patients with cardiac failure and Cheyne-Stokes respiration (Anthony et al., Currens et al)

The sensitivity of the respiratory center may be decreased by numerous local and general factors. cardiac failure, atherosclerosis of cerebral vessels, tumors and other lesions of the nervous centers, hypertension of the spinal fluid. sleep and certain drugs (morphine, etc.). Cheyne-Stokes respiration may be a normal phenomenon in children (especially in those born prematurely) and in the aged during sleep (Seherf and Boyd).

In many patients, this respiratory alteration is accentuated by the beginning of sleep, and the latter is interrupted by the phase of hyperpnea. This is one reason why certain patients with cardiac failure have great difficulty in falling asleep. However, at times Cheyne-Stokes respiration disappears when the sleep is deep, probably because in this condition, the tension of carbon dioxide in the blood is increased (East et al.). Cheyne-Stokes respiration has been observed during Stokes-Adams attacks. Hyperpnea coincides with the arrest or decrease of the ventricular rate (*Fulton's paradox*). However, in many circumstances, the opposite occurs and Cheyne-Stokes respiration produces AV block (Bullrich et al).

The mechanism by which aminophylline relieves Cheyne-Stokes respiration is not well known, although it has been attributed to a direct stimulating action on the respiratory center or to a greater local accumulation of carbon dioxide caused by reduction of cerebral blood flow (Moyer et al.).

GALLOP RHYTHM; ALTERNANS

TRIPLE AND QUADRUPLE RHYTHMS OF THE HEART

The names *triple rhythm* and *quadruple rhythm* have been suggested to indicate those cadences which are due to addition of one or two diastolic sounds to the more commonly heard two heart sounds. Older and well-known names were *gallop rhythm* and *train-wheel rhythm* The new terms are more comprehensive and include several possibilities not previously considered.

As already mentioned (Part 2, Chap 10, and Part 3, Chap. 9, Technical Aspects of Phonocardiography), the normal heart may have four sounds The two loudest are the 1st and 2d sounds, at the beginning and end of ventricular systole (*systolic sounds*), the other two, of lesser intensity, occur during ventricular diastole, respectively coinciding with the two phases of rapid filling of the ventricles (*diastolic sounds*). They are the *3d sound* (which falls at the peak of the phase of rapid, passive filling) and the *4th, or atrial, sound* (which occurs in coincidence with atrial contraction) They are usually inaudible in adults, except in persons with a flat, thin chest, who may have an audible 3d sound.

The atrial (or 4th) sound is audible on auscultation only in pathologic conditions. However, phonocardiographic tracings reveal either one or two small, low-frequency vibrations in presystole in many normal subjects, especially if they are young. These deflections have been regarded as consisting of two different components (1) a low-amplitude group of vibrations associated *with atrial contraction,* (2) a larger group, occurring 0.05 to 0.09 sec later (Weitzman), which is attributed to ventricular distention (Cossio and Braun-Menéndez; Kincaid Smith and Barlow, 1959a; Kuo et al.; Leonard et al). This second group has also been related to tensing or closure of the AV valves *before* the onset of ventricular contraction (T. Lewis), and actual, though not completely convincing, evidence for such movements has been reported by several authors (Little; Little et al , Ankeney et al., Moscovitz and Wilder; Yoshida et al , 1960).

Since contraction of the right atrium precedes that of the left, it is logical to assume asynchronism between right and left atrial sounds. This may further confuse the correlation with mechanical events.

In an experimental study correlating intracardiac pressures with intracardiac sounds, Muresan et al. concluded that the first group of vibrations was due to atrial contraction, and the second, to ventricular filling However, a short reversal of pre-

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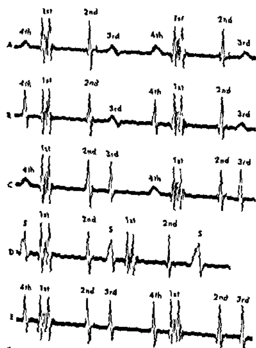


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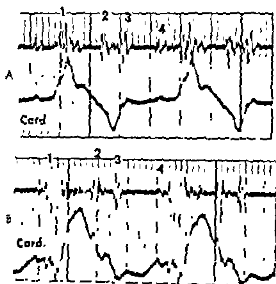


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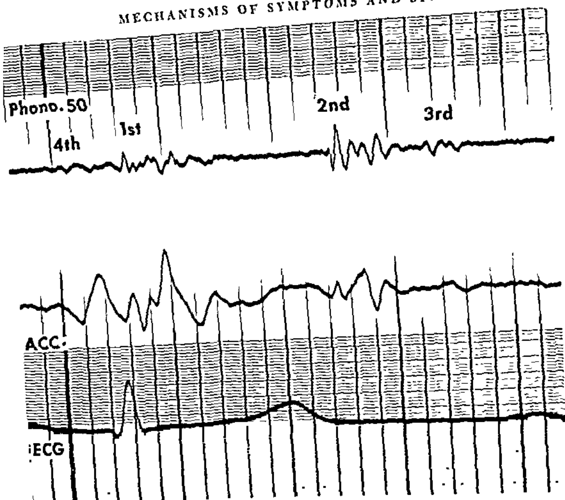


Fig 5-11. Normal subject Phonocardiogram (filter at 50 cps) (above), acceleration tracing of the precordium (center), and electrocardiogram The acceleration tracing reveals better than the phonocardiogram the large presystolic wave that coincides with the 4th sound.

apex and then at the epigastrium (or 3rd left interspace), or simultaneously over both areas, reveal whether the triple rhythm originates in the left or in the right ventricle. A triple rhythm recorded *only at the apex* usually reveals left ventricular strain; a triple rhythm recorded *only at the epigastrium* usually reveals right ventricular strain In exceptional cases, triple rhythms are recorded over *both* areas (Fig. 5-12), indicating biventricular strain

The following conditions increase the loudness of the diastolic sounds:

1. *Rapid heart action.* The short diastole causes a tumultuous filling of the ventricles

2. *Prolonged interval between atrial and ventricular contractions* The increased interval permits a better audition but does not change the graphic characteristics of the atrial sound

3 *Hypertrophy of the left atrium*, as observed in mitral insufficiency without marked mitral stenosis, is the cause of a powerful atrial contraction, which displaces a large amount of blood. The same is true for the *right atrium* in cor pulmonale or severe mitral stenosis with relative tricuspid insufficiency or in cases of organic tricuspid insufficiency or atrial septal defect. In these cases, there is an increase of the 3d sound.

4 *Dilated and weak myocardium.* The ventricular wall has greater vibration when hit by the fluid wave. This is common in congestive failure and in coronary heart disease.

5. *Ventricular strain* favors triple rhythms through increase of left ventricular diastolic pressure and atrial filling pressure; this is typical of hypertensive heart disease with left ventricular strain

The reason similar conditions may cause large 3d or 4th sounds tentatively may be explained as follows

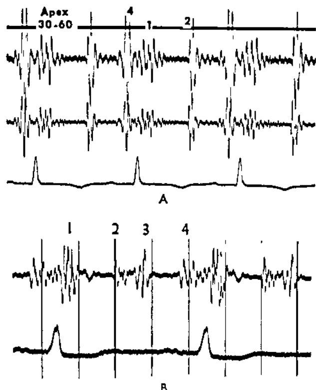


Fig 5-8. A Hypertensive heart disease Phonocardiograms at apex and ECG. *From above* Filtered phonocardiogram (30 to 60 cps) "Stethoscopic" phonocardiogram ECG *Triple rhythm* due to large 4th sound in presystole B Coronary heart disease Heart failure. *Quadruple rhythm* due to large 3d and 4th sounds. Each of these diastolic sounds is followed by a short rumble (Upon auscultation impression of a diastolic rumbling murmur)

sion, of the 3d with the 4th sounds (Fig 5-9)

When diastole is long (bradycardia), and both the 3d and 4th sounds are large, one may observe.

4. *Quadruple rhythm.* There are two additional sounds in diastole, representing the accentuation of *the 3d and 4th sounds* (Fig 5-7A), which are separated from each other.

Each diastolic sound is made of a high diphasic or triphasic vibration when recorded with a "stethoscopic" system or a filtered system in the low range (30 to 69 cps). In higher bands (60 to 120 or 120 to 140 cps), occasionally two to three small rapid vibrations may be recorded The extra sound is simultaneous with a high wave in the ultra-low-frequency tracing (linear cardiogram at apex and epigastrium). In the summation type, two distinct waves may be present in the ultra-low-frequency tracing, even if a prolonged sound or short rumble is revealed by the sound tracing

Occasionally, pathologic 3d or 4th sounds, or a summation sound, can be recorded even in the 240 to 480 cps range (Luisada and Di Bartolo) (Fig. 5-10).

The acceleration tracing at the precordium (range, 5 to 25 cps) reveals the diastolic vibrations better than any other type of tracing Sometimes these vibrations are recorded by such a method even when the conventional phonocardiogram fails to reveal them (Rosa and Kunos) (Fig. 5-11).

Phonocardiograms recorded first over the

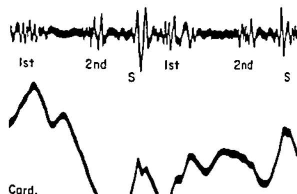


Fig 5-9. Phonocardiogram (stethoscopic) and low-frequency tracing (cardiogram) at apex in chronic glomerulonephritis with severe hypertension *Summation type* of triple rhythm The additional sound S corresponds to a diastolic forward thrust in the low-frequency tracing.

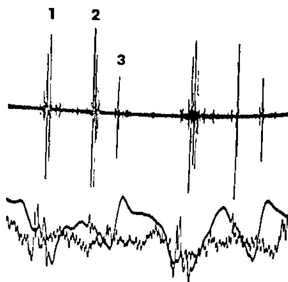


Fig 5-10. Triple rhythm due to early-diastolic additional sound in a 14-year-old boy with myocarditis *From above.* Phonocardiogram (range, 200 to 400 cps), ultra-low-frequency tracing at apex, ECG (muscular tremor). (*From Luisada and Di Bartolo, Am. J. Cardiol*, 1961)

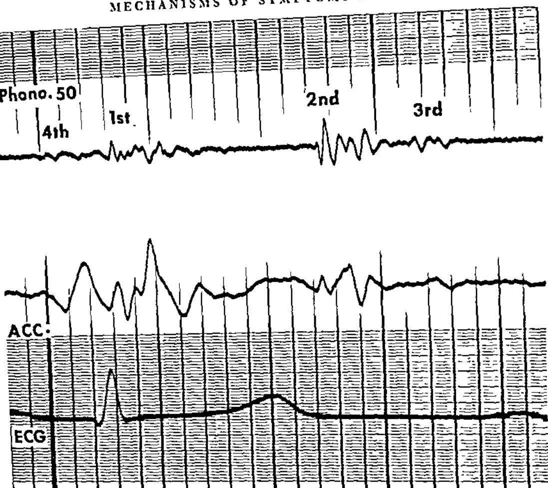


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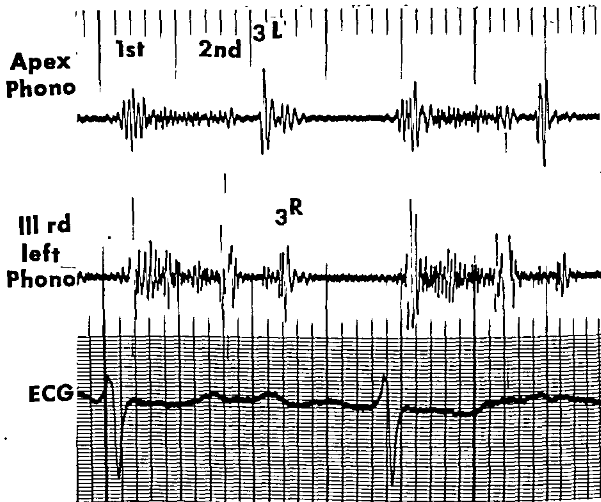


Fig. 5-12. Biventricular triple rhythm (right and left gallop). Simultaneous phonocardiograms at apex and midprecordium in severe mitral insufficiency The large 3d sound at apex (left ventricle) precedes that at the midprecordium (right ventricle).

a A large 4th sound occurs when the diastolic pressure rises in one ventricle and the respective atrium increases the power of its contraction (left or right ventricular failure-atrial systolic overload).

b A large 3d sound occurs when the filling of an atrium is increased (atrial septal defect, tricuspid insufficiency, mitral insufficiency-atrial diastolic overload).

A *diastolic type of triple rhythm*[5] is recognized by recording simultaneously a phonocardiogram and an ultra-low-frequency (linear cardiogram) or a low-frequency (accelerogram) tracing at the apex or epigastrium. The atrial type is also well recognized by comparison with an electrocardiogram: the additional sound precedes the QRS complex.

In differential diagnosis between splitting of the 2d sound, opening snap of the mitral valve, and a diastolic sound, apart from the time coincidence with the waves of the low-frequency tracing (cardiogram) and the electrocardiogram, one may also make use of the following average figures for adults (the intervals are shorter in children)

1 The distance between the two phases of a split 2d sound varies between 0.025 and 0 05 sec (this interval was formerly thought to be 0 03 to 0 11 sec, but the last figure should not be accepted)

2. The distance between the aortic component of the 2d sound and the opening snap of the mitral valve varies in adults between 0.06 and 0.11 sec (formerly thought to be 0.07 to 0 13).

3. The distance between the aortic component of the 2d sound and the beginning of the 3d sound varies between 0.12 and 0 18 sec.

A dull *3d sound* is normal in children or

[5] Addition of a sound in systole causes a *systolic type of triple rhythm*

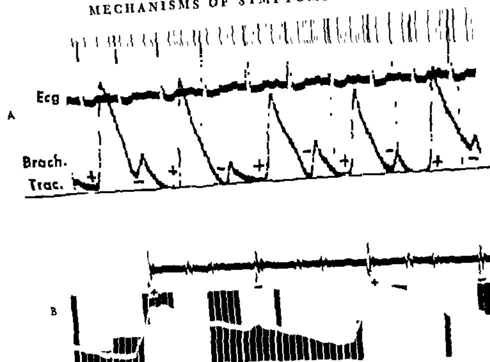


Fig. 5-13. Pulsus alternans A. ECG and brachial pulse tracing. The pulse presents severe alternation. The ECG has phasic respiratory variations but no alternans. B. Phonocardiogram over aortic area and brachial pulse tracing There is alternation of the pulse and of the 2d aortic sound.

young persons with a thin, flat chest *It is* abnormal in older persons or if it is very large. A *4th sound* may be recorded (seldom heard) in normal subjects above the age of 40. It becomes an abnormal phenomenon if it is found in younger persons or if the vibration is large or high-pitched

As already stated, triple and quadruple rhythms are commonly associated with tachycardia, ventricular dilatation, or ventricular strain Therefore, these rhythms are frequently encountered in pregnancy, thyrotoxicosis, fever, anemia, constrictive pericarditis, rheumatic or congenital heart diseases, and hypertensive or coronary heart diseases *They are also typical of heart failure.* They are frequently found after a myocardial infarct. The rhythm is caused by functional phenomena, which may disappear (delivery, sedation, digitalization, mitral surgery, sympathectomy, or venesection), causing a return to normal of the auditory phenomena

While a triple rhythm is more frequent in patients with cardiac disease than in normal subjects, it may be found occasionally even in the latter because its production is favored by functional elements that may be present without heart disease.

The term "triple rhythm" should be preferred to others in order to dispel the unjustified fears once attached to the term "gallop rhythm." However, it should be kept in mind that a triple rhythm is evidence of a definite *functional* disturbance of the heart.

One important observation is that, *in heart failure*, mechanical systole may have a different duration from that of electrical systole (Hegglin). This is typically revealed by comparing a phonocardiogram with an electrocardiogram. The description of this phenomenon can be found in Part 18, Chap. 9.

ALTERNANS

Pulsus alternans occurs when every other pulse wave is weak although there is no irregularity of the heart (Fig 5-13).[a] It may appear during attacks of paroxysmal tachycardia. It is typical of hypertension, coronary heart disease (especially after myocardial infarction), and congestive failure.

Pulsus alternans is recognized by palpation of the radial pulse only when it is exceptionally

[a] Recent studies have shown that it is possible to recognize alternans even when the heart rhythm is irregular.

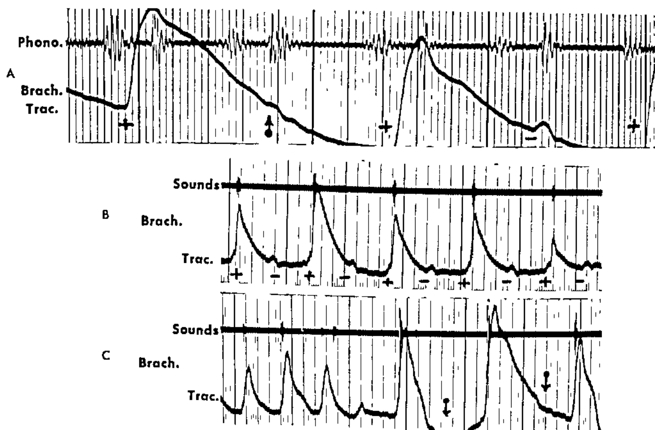


Fig. 5-14. A. Phonocardiogram and brachial tracing at 90 mm. Alternation of heart sounds (discordant alternation of the 1st sound, concordant alternation of the 2d sound). There is a questionable pulse wave in cycle 2, and a more visible one in cycle 6 B, C. Brachial tracings *Above* arterial sounds. *Below* arterial pulses Both are simultaneously recorded by two crystal microphones from a recording cuff inflated at 25 mm The compressing cuff had a pressure of 90, equivalent to diastolic pressure Cycles 2, 4, 6, 8, and 10 of tracing B have an extremely small pulse wave but no arterial sound (stethoscopic halving) In tracing C, a deep respiration disturbs the sequence, causing larger pulses. cycles 6 and 8 have no pulse and no arterial sound (sphygmographic and stethoscopic halving) (*From Liu and Luisada. Am Heart J*, 1955.)

severe. Manual compression of the brachial artery may cause halving of the pulse, thus revealing less-marked alternation

Blood pressure tracings easily reveal the alternans. If the patient has a heart rate of 60, decompression first shows the arterial sounds due to the large waves (rate of 30), then those due to all waves (rate of 60). A new halving of the rate may be observed near the level of diastolic pressure.

There are four types of alternating pulse (1) alternation of the peak (systolic alternation); (2) alternation of the foot (diastolic alternation), (3) alternation of both (systolic and diastolic alternation); (4) alternation of the dicrotic wave. In exceptional cases, the tibial tracing fails to reveal an alternation that is present in the brachial tracing

Several phenomena may alternate in pulsus alternans:

1 The intensity of the cardiac sounds, chiefly the 2d (Fig. 5-14)

2 The intensity of a murmur

3 The amplitude of the ventricular contractions as recorded by the electrokymograph (Fig 5-15)

4 The amplitude of the pressure pulse of either the right or the left ventricle, as well as the pulses of either the aorta or the pulmonary artery

In rare cases, alternation may be so severe that the small pulse disappears Then, there is *halving of the pulse* (Figs 5-13 and 5-14), a phenomenon that has been called *pulsus bisectus* (Liu and Luisada, 1955)

At times, the electrocardiogram reveals an alternation of P, R, T, or S–T, which may be *concordant* or *discordant* in relation to the pulse

Exertion usually increases the alternation

A premature beat may start the alternation, which usually continues for some time thereafter.

Differential diagnosis from a bigeminal pulse is made by observing an electrocardiogram and a pulse tracing. The ventricular complexes are identical in pulsus alternans, the unusual complex of a premature contraction periodically follows a normal complex in bigeminal pulse. The small wave is often nearer the preceding large wave in bigeminal pulse.

In certain cases with rapid respiration, the cardiac rate may be only twice the respiratory rate, simulating alternation of the pulse. Asking the patient to "hold his breath" for a few seconds reestablishes equal pulses.

Mechanism. Alternation of various cardiac functions has been described. *Alternating conductivity* leads to periodic changes of the P-R interval or to periodic AV block every second beat, and may cause an alternating bundle branch block. *Alternating automatism* has been advocated as the cause of bradycardia, similar to that of periodic SA block type 2:1. Similarly, *alternation of the strength of ventricular systole* is the cause of pulsus alternans.

The most likely explanation is the following. A certain area of the ventricular myocardium (or a certain number of fibers here and there) possesses a *longer refractory period* than the rest of the heart, either because it has been damaged or because its blood supply is poor. When a stimulus reaches the ventricle after a long pause (respiratory arrhythmia, compensatory pause after a premature beat, or during slow rate caused by vagal reflex), *all fibers contract, causing a large blood wave to enter the aorta.* However, this contraction is followed by a diastole that is not sufficiently long to restore the damaged fibers. The following stimulus causes the contraction of all fibers, *except those damaged* (which are still in a relatively refractory period), whereupon a *small blood wave enters the aorta.* Then a large and a small wave alternate again until a change occurs in the heart rate or in the conditions of the myocardium. In other words, a difference in the length of the refractory period of some fibers

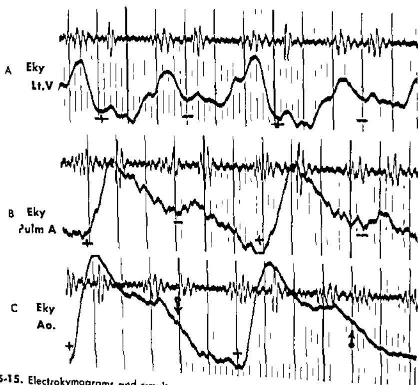


Fig 5-15. Electrokymograms and simultaneous sound tracings. A. Left ventricular border in pulsus alternans. Alternation of diastole and systole with smaller waves in cycles 2 and 4. B. Pulmonary knob. Alternation of pulmonic pulses. C. Aortic knob. Complete halving of the pulse. The small waves of cycles 2 and 4 should appear at the time of the 2d sounds (arrows). (From Liu and Luisada, Am Heart J., 1955.)

makes it possible that they contract only every other stimulus while all other fibers contract with every stimulus. Pulsus alternans indicates that a large number of cardiac fibers are in an abnormal functional condition. However, if the damaged fibers are in an area that has little or no influence on the size of the pulse, only other manifestations of cardiac activity reveal the disturbance, or it may not be apparent.

It is possible that pulsus alternans is caused occasionally by alternating changes in the tonus of the aorta and even in the tonus of one or more peripheral arteries Proof of this, however, is not altogether convincing.

Diagnosis. Diagnosis of pulsus alternans is simple if it is remembered that it is a *regular pulse* with alternately smaller and larger waves. The phenomenon can be recognized by several maneuvers (manual compression of the brachial artery, inflated blood pressure cuff, exertion).

Differential diagnosis from a *bigeminal pulse* is easy with the aid of simultaneously recorded electrocardiogram and pulse tracing. The ventricular complexes are identical in pulsus alternans, while the complex of a premature contraction periodically follows a normal complex in bigeminal pulse. The small wave is *nearer the following large wave* (or is at an equal distance) in pulsus alternans; it is *nearer the preceding large wave* in bigeminal pulse.

In certain cases, if respiration is rapid, the cardiac rate may be one-half the respiratory rate. This may cause a nonpathologic alternation of the pulse. Asking the patient to "hold his breath" for a few seconds reestablishes equal pulses.

Prognosis. The pulsus alternans of paroxysmal tachycardia, and that occurring for only five to six contractions after a premature beat, are of limited importance. Nevertheless, they add severity to the syndrome. The pulsus alternans of all other conditions has a serious prognosis Its importance should be evaluated together with all other clinical data, but there is no doubt that pulsus alternans is a serious sign.

Disappearance of pulsus alternans in a hypertensive patient, after surgery on the sympathetic system, treatment by hypotensive drugs, or thyroidectomy has been observed by the author and is evidence of marked improvement.

1

;tiology and pathogenesis f congenital heart disease

MAURICE LEV AND ELISABETH KAVEGGIA

ETIOLOGY

The etiology of congenital heart disease is today unknown Various etiologic factors have been advanced as responsible in individual cases They are (1) maternal factors, (2) genetic factors, (3) hypoxia and placenta previa, and (4) mongolism.

Maternal Factors There is some evidence that there is an increased occurrence of congenital heart disease in the offspring of mothers over 40 years of age (Polani et al, Malpas) Likewise, there is a possible increase with the greater number of pregnancies (Lamy et al) However, there is no evidence that chronic illness in the mother predisposes to congenital heart disease (Hartmann et al, Richards et al) *Rubella* in the mother in the first trimester (Swan et al; Wesselhoeft, Gregg, Ericson, Rutstein, and Albaugh), or even up to 3 months before gestation, is a definite factor in some cases (Swan, 1949), but of doubtful importance in the majority of instances (Lundstroem, Greenberg et al., Gibson) The abnormality frequently produced with rubella is patent ductus Associated eye findings are frequent *Herpes* simplex in the first trimester has been associated with occasional cases of tetralogy of Fallot (Richards et al) Although general nutritional status of the mother may be a factor in the production of other abnormalities (Buerke et al, Stuart, Sandrucci), there is no evidence that this factor is related to congenital heart disease Likewise, there is definite evidence that *irradiation of the mother* may be related to the production of abnormalities in the fetus (Murphy, 1928 and 1929), but only an occasional case of congenital heart disease can be ascribed to this *Gynecologic disorders* may be associated with mongolism and congenital heart disease (Ingalls, 1947; Lamy et al.)

Genetic Factors. Some cases of congenital heart disease appear to have a *genetic etiology* (Medvei and Roesler, Mildenberger, Jex, Blake, Stein and Barker, McKeown *et al.*). Cases have been reported where father and son both had coarctation, two sisters both with Lutembacher's complex, three sisters with patent ductus, coarctation in the mother and patent ductus in two children, the same type of ventricular septal defect in the mother and in her 6-months-old fetus, hypoplasia of the aortic tract complex in two siblings, patent ductus in all six siblings. Likewise, *consanguinity* appears to be a factor in some cases

Other Etiologic Factors. It has been clinically observed in one locality that patients suffering from patent ductus are more commonly born at higher altitudes than at sea level (Haring) This suggests a possible *hypoxic factor* Although placenta previa (Greenhill) and placental infarction (Talbot) are associated in some cases with other abnormalities, there is no evidence that they are related to congenital heart disease. *Mongolism* is definitely associated with congenital heart disease, especially com-

mon AV orifice, atrial septal defects, and transposition of the great vessels.

Experimental Production of Congenital Heart Disease. Congenital heart disease has been produced experimentally by (1) hypoxia in the fetus, (2) vitamin-A deficiency in the mother, (3) deficiency in pteroylglutamic acid in the mother, (4) administration of trypan blue and other azo dyes to the mother, and (5) irradiation of the fetus.

HYPOXIA. Many types of anomalies have been produced by hypoxic means, but congenital heart disease was found in only one series (Ingalls et al). In this series, of 210 pregnant mice suffering hypoxia in 5 5 days of pregnancy, four fetuses showed ventricular septal defect, in three of which it was combined with other abnormalities

VITAMIN A DEFICIENCY. Cardiac anomalies were produced in 28 of 64 newborn rats by vitamin A deficiency in the mother (Wilson and Warkany). The anomalies found were defect of ventricular and aortopulmonary septum and aortic arch malformations These anomalies could be prevented by administration of vitamin A prior to the twelfth day of pregnancy (Wilson et al., 1953).

DEFICIENCY OF PTEROYLGLUTAMIC ACID Deficiency of pteroylglutamic acid in the mother produced the following cardiac anomalies ventricular septal defects, truncus arteriosus communis persistens, double or right aortic arch, absence of the ductus arteriosus, and aberrant origin of the subclavian arteries (Baird).

TRYPAN BLUE. The injection of trypan blue into pregnant rats has repeatedly produced congenital anomalies of the heart The anomalies produced were ventricular septal defect, atrial septal defect, patent ductus, pulmonary stenosis or atresia (Rich-[illegible]

duced a pathologic complex consisting of displacement of both atria, elongation of the heart, counterclockwise rotation of the heart, ventricular septal defect, dextroposition of the aorta, and pulmonary stenosis The dye acts probably by altering the maternal metabolism since the dye is not found in the placenta or fetus, but in the reticuloendothelial system of the mother (Fox and Goss).

IRRADIATION Irradiation of rat embryos directly through the abdominal incision of the mother caused the following developmental defects. situs inversus, failure of development of the foramen secundum, transposition of the great vessels, right or double aortic arch, truncus communis, atrial and ventricular septal defects, and common AV orifice (Wilson et al, 1953).

HORMONES. Although abnormalities have been produced by the administration of ACTH, cortisone (Fraser and Feinstat), and anterior pituitary extract (Fraser and Feinstat), no congenital heart disease has been found to date.

PATHOGENESIS

Although the etiology is obscure, it can be assumed that some factor acts during the first two months of pregnancy to produce an abnormality in the development of the heart. This abnormality may be considered to be purely *embryologic,* or, in addition, a *phylogenetic factor* may be assumed to be operating in the production of some abnormalities It is therefore essential to introduce the subject with a brief summary of the development of the heart phylogenetically and embryologically.

Phylogenetic Development of the Vertebrate Heart. The evolution of the mammalian heart is part of the evolution of the circulation of vertebrates, which is related to the progress of life as it emerged from sea water to fresh water and from fresh water to land The outstanding characteristics of terrestrial habitat are (1) the presence of a relatively tremendous amount of oxygen in the atmosphere, (2) the low viscosity of the air, permitting rapid motion, (3) the marked fluctuations in temperature, and (4) the relative absence of water. The development of the circulation of vertebrates, although correlated with adaptations to all these environmental factors, was mostly related to the increasing ability to utilize oxygen

With a change from a water to a land environment, lungs were developed with a gradually increasing amount of respiratory epithelium This made possible increased absorption of oxygen and increased liberation of carbon dioxide, greater than that possible in gill-bearing vertebrates. This in turn resulted in fundamental changes in the transport of these substances and in the giving of the one and the removal of the other from the body cells There thus ensued marked changes in the physiology and morphology of the circulation. The physiologic changes were (1) an increased efficiency of the pump, (2) an increase in the oxygen-carrying capacity of the blood, and (3) an increase in oxygen tension The increased efficiency of the pump was obtained by (1) an increase in pressure, (2) an increase in speed of transmission of the excitation process, (3) an increase in heart ratio, and (4) an increase in rate. All these may be said to have been catalyzed mostly by the oxygen in the atmosphere and the circumstances available for its utilization, reinforced by homeothermism in birds and mammals (Clark)

The associated morphologic changes concerned

themselves mostly with the heart. The evolution in cardiac structure in vertebrates involves a change from the *single circulation* found in the *fish* with a four-chambered heart, whose chambers are arranged in series, to a *double circulation* of interchanging blood, found in the *bird* and *mammal* with a four-chambered heart, two of whose chambers are arranged in parallel to the other two (Spitzer). This remarkable change is brought about in two phases of development (Pernkopf and Wirtinger).

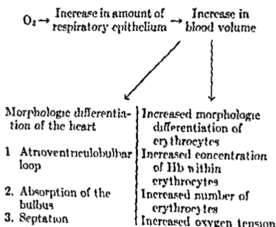
In the first phase, the straight-tubed heart bends and twists upon itself in the form of an atrioventriculobulbar loop and bayonet-shaped bulbus. Concomitant with this is the beginning formation of septa and cushions in the atria and bulbus. This is as far as the development proceeds in the *amphibia*. In the second phase, the bulbus is absorbed into the ventricles. Concomitant with this is the completion of septation, the reorientation of the atria and ventricles, the absorption of the sinus venosus, and the development of valves. In *reptiles*, this process proceeds only partially, with incomplete septation in the ventricles. In *birds* and *mammals*, the complete separation of the circulations occurs.

The transition from the reptilian to the mammalian stage of circulatory development is important for the understanding of congenitally abnormal hearts. In the reptilian truncus, two septa develop, a *septum aorticopulmonale* and a *septum aorticum*, which eventually divide the vessel into three parts—two aortas and a pulmonary artery. In the mammal, only a *septum aorticopulmonale* develops, dividing the truncus into two vessels—a single aorta and a pulmonary artery. Likewise, in the reptilian bulbus, three ridges develop (1A, 4B, and 3C), which eventually form two septa, dividing the bulbus into three coni, one for each aorta and one for the pulmonary artery. In the mammalian bulbus, only two ridges develop (1A and 3B), which ...
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There is some evidence in favor of the hypothesis that hydrodynamic factors are in part responsible for the changes in the circulation in the ascending series of the vertebrates. These are the progressive increase in blood volume and pressure, catalyzed and augmented by the development of lungs. The increase in volume and pressure might be responsible for the initial division of the cardiac tube into sinus venosus, atrium, ventricle, and bulbus; the subsequent absorption of the bulbus and sinus venosus, and the formation of septa throughout the heart tube (Diagram 6-1) (Spitzer, Lev and Saphir, 1945).

DIAGRAM 6-1. PHYLOGENETIC AND ONTOGENETIC DEVELOPMENT OF THE CIRCULATION



Lev's modification of Spitzer's theory of the development of the circulation in vertebrates.

The Embryologic Development of the Heart.[1] The human heart arises from paired primordial thickenings in the splanchnic mesoderm, situated lateral to the primitive pharynx. From a proliferation of these cardiogenic plates, cells become separated and form elongated endothelial tubes on each side of the primitive gut. Two constrictions subsequently divide these tubes into three parts, a cephalic or bulbar, a middle or ventricular, and a caudal atrial region. With the formation and separation of the floor of the foregut from the yolk sac, the endothelial tubes swing medialward and progressively fuse ventral to the foregut anteriorly and posteriorly. Above and below this fused endothelial tube, the cardiogenic plates likewise come together, forming the epimyocardial mantle. The fusion of the cardiogenic plates dorsally forms the dorsal mesocardium. No ventral mesocardium is formed in the human embryo. The dorsal mesocardium subsequently disappears, and the heart is now freely suspended in the adjacent primitive coelom, which thus forms the pericardial cavity. At this stage, the heart consists of a tubular structure made up of the following (1) the bulbus, (2) the primitive ventricle, (3) the primitive

[1] See also Part 1, Chap. 1, ...

mon AV orifice, atrial septal defects, and transposition of the great vessels.

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TRYPAN BLUE The injection of trypan blue into pregnant rats has repeatedly produced congenital anomalies of the heart The anomalies produced were ventricular septal defect, atrial septal defect, patent ductus, pulmonary stenosis or atresia (Richmann). Other azo dyes, such as Evans blue, Niagara blue 4B, and Niagara blue 6B, have a lesser teratogenetic effect (Wilson, 1955).

In one series, the injection of trypan blue produced a pathologic complex consisting of displacement of both atria, elongation of the heart, counterclockwise rotation of the heart, ventricular septal defect, dextroposition of the aorta, and pulmonary stenosis. The dye acts probably by altering the maternal metabolism since the dye is not found in the placenta or fetus, but in the reticuloendothelial system of the mother (Fox and Goss).

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In the first phase, the straight-tubed heart bends and twists upon itself in the form of an atrioventriculobulbar loop and bayonet-shaped bulbus. Concomitant with this is the beginning formation of septa and cushions in the atria and bulbus. This is as far as the development proceeds in the *amphibia* In the second phase, the bulbus is absorbed into the ventricles. Concomitant with this is the completion *of septation, the* reorientation of the atria and ventricles, the absorption of the sinus venosus, and the development of valves In *reptiles, this process proceeds* only partially, with incomplete septation in the ventricles In *birds* and *mammals*, the *complete* separation of the circulations occurs

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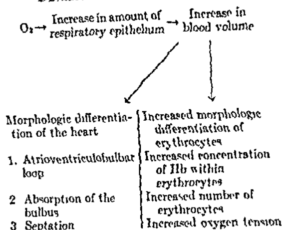
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There is some evidence in favor of the hypothesis that hydrodynamic factors are in part responsible for the changes in the circulation in the ascending series of the vertebrates *These* are the progressive increase *in* blood *volume* and pressure, catalyzed and augmented by the development of lungs The increase in volume and pressure might be *responsible* for the initial division of the cardiac tube into sinus venosus, atrium, ventricle, and bulbus; the subsequent absorption of the bulbus and sinus venosus, and the formation of septa throughout the heart tube (Diagram 6-1) (Spitzer; Lev and Saphir, 1945).

Diagram 6-1. Phylogenetic and Ontogenetic Development of the Circulation



Lev's modification of Spitzer's theory of the development of the circulation in vertebrates

The Embryologic Development of the Heart.[1] The human heart arises *from paired* primordial thickenings in the splanchnic mesoderm, situated lateral to the primitive pharynx. From a *proliferation of these cardiogenic* plates, *cells* become separated and *form* elongated endothelial tubes on each side of the primitive gut Two constrictions subsequently *divide* these tubes into three parts a cephalic or bulbar, a middle or ventricular, and a caudal atrial region. With the formation and separation of the floor of the foregut from the yolk sac, the endothelial tubes swing medialward and progressively fuse *ventral to the foregut* anteriorly and *posteriorly* Above and below this fused endothelial *tube*, the cardiogenic plates likewise come together, forming the epimyocardial *mantle* The fusion of the cardiogenic plates dorsally forms the dorsal mesocardium. No ventral mesocardium is formed in the human *embryo. The dorsal* mesocardium subsequently disappears, and the heart *is* now freely suspended *in* the adjacent primitive coelom, which thus forms *the pericardial* cavity At this stage, the heart consists of a tubular structure made up of the following. (1) the bulbus, (2) the primitive ventricle, (3) the *primitive*

[1] See also Part 1, Chap 1. *Editor*

atrium, and (4) the sinus venosus. The truncus arises from the bulbus and, at this stage, is connected to the dorsal aorta by the first aortic arches (Arey, Patten, Jordan and Kindred; Hamilton et al.).

The development of the heart from this point may be divided into two phases, as in phylogeny. (1) the formation of the atrioventriculobulbar loop and (2) the absorption of the bulbus (Arey; Patten; Jordan and Kindred; Hamilton et al.; Odgers; Pernkopf and Wirtinger).

PHASE I Up to about 7 mm because of the relatively greater growth of the heart than that of the containing cavity, and because its cranial and caudal ends are fixed by the aortic arches and the septum transversum, respectively, the cardiac tube twists upon itself in three dimensions to form the complex atrioventriculobulbar loop (or bulboventricular loop). During this formation, torsions of 90° occur at the atrioventricular and ventriculobulbar orifices in such a way as to approximate their mesocardial walls (Pernkopf and Wirtinger)

At 4 to 5 mm of fetal length, the anlage of the septa begins to be laid down on all portions of the heart tube—the septum primum, the endocardial cushions, the main ventricular septum, the proximal bulbar cushions A and B, the distal bulbar cushions 1 to 4, and the truncus spurs. Although each of these must be dealt with separately, they are all simultaneous parts of the process of septation, related to the formation of the atrioventriculobulbar loop

PHASE II. This phase concerns itself mostly with the *absorption of the bulbus,* but includes the absorption of the sinus venosus and changes in the atrial canal region According to Pernkopf and Wirtinger, the absorption of the bulbus is affected by two processes. A torsion of 150° (counterclockwise looking truncusward from the bulbus) occurs at the bulbotruncal ostium and a back torsion of about 45° (clockwise looking bulbusward from the ventricle at the ventriculobulbar ostium). These torsions unwind the bulbus and telescope it. This is accompanied by a deviation of the bulbus to the left and ventrally. The changes in the bulbus are associated with simultaneous changes in the atrial canal. This canal shifts to the right and dorsally, so that the bulbus sinks into the groove between the developing mitral and tricuspid valves. In this way, the bulbus is absorbed into the ventricles, its aortic portion disappearing as a separate entity while its ventral portion assumes the role of conus of the right ventricle. During this phase, septation is completed in all parts of the cardiac tube.

Simultaneous with the absorption of the bulbus occurs the absorption of the sinus venosus and the common pulmonary vein The *sinus venosus* is divided into right, left, and transverse portions or horns. The left horn early becomes smaller than the right, because of a shift of venous blood from the left to the right side. From 10 to 20 mm, the sinus lags behind the growth of the right atrium so that the right horn is absorbed into the latter. The transverse portion becomes the coronary sinus, while the stem of the vein of Marshall is the only remnant of the left horn. The eustachian and thebesian valves are remnants of the right valve of the sinus venosus The linea terminalis demarcates that portion of the right atrium arising from the sinus and that portion comprising the primitive right atrium The absorption of the common pulmonary vein will be dealt with below

THE ATRIAL SEPTUM At 4 to 5 mm, the septum primum appears in the cephalodorsal wall of the primitive atrium growing ventrocaudally. The residual foramen between the resulting atria adjacent to the endocardial cushions is the foramen primum At 6 5 mm, the dorsal component is met by a small ventral component Cranially, at 8 to 9 mm, there is a defect in union of these components, with the production of the foramen ovale I. With the fusion of the endocardial cushions, the latter grow to meet the *septum primum,* thus eliminating the *foramen primum* (10 to 12 mm)

The *septum secundum* is likewise developed from dorsal and ventral components (9 to 18 mm) The dorsal is the primordial septum secundum and the left valve of the sinus venosus (possibly including the septum spurium) The ventral is the septum intermedium which is an extension of the fused endocardial cushions The opening in this septum primum and secundum results in their overlapping and makes possible the closure of the foramen ovale I and II after birth

The foramen ovale becomes physiologically closed at birth almost instantaneously It becomes anatomically so by 1 year of age. In about 25 per cent of instances, it may remain

obliquely probe patent The physiologic closure is probably affected as follows: with the onset of respiration there is a fall in pulmonary pressure and an increase in pulmonary and left atrial flow. The increase in pressure in the left atrium produces the approximation of the overlapping two atrial septa

THE MITRAL AND TRICUSPID ORIFICES AND VALVES. At 4 to 5 mm, the dorsal and ventral endocardial cushions form on the common AV canal. At this stage, this canal is situated to the left of the bulbus. Later (11 mm), right and left lateral endocardial cushions make their appearance. The right lateral cushion is apparently formed from the proximal bulbar swelling B or its junction with the fused anterior and *posterior endocardial cushions.* At about 11 mm, the anterior and posterior endocardial cushions fuse, forming the mitral orifice and the tricuspid orifice, and about the same time the cushions send an extension up to fuse with the septum primum, obliterating the foramen primum.

The division of the mitral and tricuspid orifices occurs while the entire atrial canal shifts posteriorly and to the right behind the ventrally advancing bulbus Thus the mitral and tricuspid orifices are formed during the absorption of the bulbus

The development of the *mitral* and *tricuspid valves* occurs in three periods (Odgers). In the first period (11 to 23 mm), the various leaflets are first derived as follows The inferior leaflets of the mitral and tricuspid valves are formed from the lateral endorcardial cushions (11 mm), the aortic leaflet of the mitral from the fused anterior and posterior cushions (11 4 mm), the anterior leaflet of the tricuspid from the fused anterior and posterior cushions and the right proximal bulbar swelling B (11 4 to 14 5 mm), and the septal cusp of the tricuspid from the posterior endocardial cushion (15 5 mm) During this period, the leaflets consist of cushion material and muscular trabeculae, with the former predominating

In the second period (23 to 61 mm), muscle gradually invades and replaces cushion material During this stage, correlated with changes in the *pars membranacea*, the developing tricuspid leaflets migrate to become more distal than the mitral leaflets In the third period (85 mm to 4 months), collagenous tissue invades
he muscle

THE VENTRICULAR SEPTUM AND THE AORTA AND PULMONARY ARTERIES AND VALVES. At 7 mm the main ventricular septum appears, growing upward toward the endocardial cushions. The main septum fuses with the dorsal endocardial cushion to the right of its mid-point by 8 to 9 mm This leaves a large interventricular foramen.

In the meantime, the aorta and pulmonary artery are developed distally from the left fourth and sixth aortic arches and proximally from the division of the primitive truncus. The latter occurs through the growth of the aortopulmonary septum. This is produced by the fusion of the spurs between the fourth and sixth arches; the septum proceeds caudally as an arched membrane, sending ahead longitudinal ridges as forerunners

At the same time, the bulbar septum has been developing from distal bulbar swellings 1 and 3 and ridges 1A and 3B (Pernkopf and Wirtinger). By 10 mm, the aortopulmonary septum has bisected bulbar swellings 1 and 3, which have fused in their centers. With the absorption of the bulbus, the proximal bulbar septum is developed, and this septum is brought into alignment with the main ventricular septum described above (10 to 20 mm). This leaves a small opening between the ventricles, which is filled in by the endocardial cushions, the bulbar cushions, and perhaps some connective tissue which covers the main muscular ventricular septum to form the pars membranacea (15 to 20 mm) (Odgers) (Fig. 6-1).

The peculiar position of the *pars mem-*

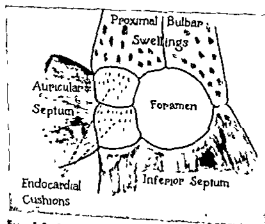


Fig. 6-1. Diagrammatic sketch of elements involved in the final closure of the interventricular foramen.

branacea between both ventricles, and also between the right atrium and left ventricle, is related to the following (Hamilton et al.). The original fusion of the endocardial cushions occurs somewhat to the left of the mid-point of the cushions. The main ventricular septum joins the posterior endocardial cushion (8 to 9 mm) considerably to the right of the mid-point, while the septum primum meets the fused endocardial cushions to the left of the mid-point (10 to 12 mm). When the pars membranacea is thus formed later, a portion of this is relatively horizontal and atrioventricular. Subsequently, this portion becomes vertical and in line with the atrial and ventricular septa.

From the above, it is evident that the definitive *interventricular septum* consists of three components: a posterior septum derived from the main ventricular septum, an anterior septum derived from the bulbar septum, and a membranous septum derived mainly from the endocardial cushions.

The *aortic and pulmonic valves* are fashioned by an undermining process involving distal bulbar cushions 1, 2, 3, and 4 This yields the aortic right and left anterior coronary cusps, and the noncoronary posterior cusp, and the pulmonary right and left posterior cusps, and the anterior cusp. The anterior aortic and posterior pulmonic cusps are derived from cushions 1 and 3, the posterior aortic from cushion 4, and the anterior pulmonic from cushion 2

THE SYSTEMIC VEINS. At 3 mm, there are three series of veins in the embryo: (1) the umbilical veins draining the chorion, (2) the vitelline veins draining the yolk sac, and (3) the cardinal veins draining the embryo itself The cardinals consist of the precardinals and postcardinals uniting to form the common cardinals, which also drain the vitelline and umbilical veins. Somewhat later, the subcardinals and supracardinals develop, also draining the embryo

The transformation of the *vitelline* and *umbilical veins* is related to the development of the liver (4 to 9 mm). The growth of the liver breaks up the vitelline vessels into sinusoids with proximal and distal segments. At the same time, there is a shift of blood to the right horn of the sinus, with an atrophy of the left. The distal segments of the vitelline veins are converted into the *portal vein,* the intermediate portions remain as the *sinusoids,* while the proximal portions become the *hepatic veins,* which at this stage drain into the right horn of the sinus venosus.

With the further growth of the liver, the developing umbilical veins are rerouted through the hepatic sinusoids. There is now a disappearance of the right and proximal part of the left, with the remainder of the left persisting. A diagonal passage is now dug out through the hepatic sinusoids to form the ductus venosus. Thus at 9 mm, blood passes from the placenta through the umbilical vein through the ductus venosus into the sinus venosus.

The differentiation of the cardinal system into the superior and inferior venae cavae occurs from 4 to 22 mm. These changes are related to the development of the *kidney.* At 4 mm the pre-, post-, and subcardinal veins have developed By 11 mm, the hepatic portion of the inferior vena cava develops from the vitelline veins, and an anastomosis develops between the subcardinals. At 15 mm the supracardinals develop, and the postcardinal system begins to atrophy By 22 mm, the inferior vena cava has developed from a fusion of various parts the vitellines, the subcardinals, and the supracardinals

At about 20 mm, the *superior vena cava* is developed from the precardinal system as follows At first, an oblique cross channel (left innominate) is formed, shunting blood from the left vein across to the right. This results in the loss of the communication of the left precardinal just caudad with the left common cardinal The latter remains as the distal part of the *vein of Marshall* The right common cardinal and the right precardinal become the superior vena cava The azygos and hemiazygos are developed from the supracardinals at about 22 mm

THE PULMONARY VEIN It is generally agreed that the pulmonary vein originates from two sources. (1) a presplanchnic source consisting of a channel formed from the confluence of the vascular plexuses of the lung, which extends to the middle part of the sinus venosus without opening into it, and (2) the main pulmonary stem being an outgrowth from the heart tube There are two opinions, however, as to whether the latter originates from the

sinus venosus or from the left atrium The common pulmonary vein is developed at 5 mm.

During the second phase of the development of the heart, concomitant with the absorption of the sinus venosus into the right atrium, the common pulmonary vein is absorbed into the left atrium. This is followed by the absorption of the right and left pulmonary veins, so that definitively four separate pulmonary veins enter the left atrium

THE AORTIC ARCHES The aortic arches make their appearance as follows: first pair, 1.3 mm, second, 3 mm; third, 4 mm, fourth, 5 6 mm; and sixth, 6 mm These arches form communications between the two dorsal and ventral aortas At 7 mm, the first and second arches are obliterated. The ventral and dorsal aorta proximal to the third arches persist as the external and internal carotid arteries, respectively. The third arches form the stems of the internal carotid arteries, while the ventral aortas between the third and fourth persist as the common carotids This is the stage of development at about 10 mm. By 14 mm the dorsal aortas between the third and fourth arches atrophy. Between 14 and 16 mm, the right dorsal aorta between the subclavian and common dorsal aorta likewise is lost. Thus, the fourth left arch and common dorsal aorta now assume the topography of the definitive aorta, and the right fourth remains as the proximal part of the right subclavian (Fig. 6-2). Also at 14 to 16 mm, the right limb of the aortic sac elongates to form the innominate artery

The distal portion of both subclavian arteries and the proximal part of the left develop from the seventh segmental arteries. Throughout their development, these derivatives undergo a constant cranial migration from their position low down on the fourth arches Because of the difference in derivation of the two vessels, the left ascends more than the right At about 16 mm, the left subclavian is just distal to the ductus arteriosus. Subsequently, it assumes its definitive position proximal to the isthmus The right sixth aortic arch remains as the right pulmonary artery, while the left persists as the left pulmonary artery and ductus arteriosus

THE CORONARY ARTERIES. These vessels begin as thickenings of the aortic endothelium at 10 to 12 mm of fetal length. This is also

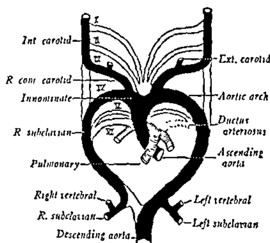


Fig. 6-2. Transformation of the human aortic arches (ventral view). Scheme with the dorsal vessels spread lateral, to show persisting vessels (black), discontinued vessels (white), and atrophic vessels (stipple) (From Arey. Developmental Anatomy. Saunders. 1954)

the time the truncus septum is bisecting the larger pair of the distal bulbar swellings, which have fused in their centers Both coronary arteries pass to the sides of the bulbus cordis, and the anterior descending coronary artery begins to be laid down. By 14 mm both circumflexes are developed, and by 20 mm all larger branches are developed

THE CONDUCTING SYSTEM.[2] There is a difference of opinion as to the method of development of the *sinoatrial node*. According to some (Walls), it can be recognized at 7 to 10 mm and is derived from sinus venosus musculature. According to others (Shaner), it appears as a new formation at 100 mm on the ventrolateral surface of the superior vena cava

The *atrioventricular node* is a derivative of the AV ring, being seen at 8 to 9 mm, at a time when the ring is still complete. It lies behind the posterior endocardial cushion. The *bundle* and the beginning of the *left branch* are recognized at about the same time and may be developed in situ or as outgrowths from the AV node By 13 mm, the right bundle appears as a similar growth, and by 22 to 25 mm the right limb can be traced into the moderator band

Nerve fibers appear in the region of the SA and AV nodes at about 21 mm.

[2] See also Part 1, Chap. 5. *Editor*

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forms of the mammal. This detorsion brings about the reopening of the right ventricular aorta. The aorta in the anomaly *overriding aorta* is thus connected with the coni of both the right and left aorta, while in partial and complete transposition, there is obliteration of the left ventricular aortic conus and persistence of the right ventricular aortic conus

In a study of the development of the heart in the bird, Bremer suggested the interpretation that the crossing of the circulations is achieved not in the bulbus, but in the atrial region He, therefore, suggested that complete *transposition* was due to the lack of formation of a kink in the atrial region, thus producing a torsion of only 90° instead of 270° in this region. This puts the pulmonary vein into the dorsal and the vena cava into the ventral portion of the heart tube The remainder of the heart tube itself is deprived of 180° torsion, and the bulbus is not kinked Thus, the aorta becomes connected with the dorsal part of the heart tube Partial transposition is due to the failure of development of the basal part of the interventricular septum and the abnormal deviation of the remainder of the septum This places the aorta into the right ventricle

Pernkopf and Wirtinger concluded that the abnormality lay in the construction *of a straight* bulbar septum, due to the *primary* development of straight ridges between the bulbotruncal ostium and the *ventriculobulbar* ostium The incorporation of a bulbus *with such* ridges into the ventricles *is not* accompanied by the normal *torsion* at the bulbotruncal ostium, and therefore the aorta and pulmonary artery are transposed Bredt considered the dextroposition of the aorta in *tetralogy of Fallot* the result of the septal defect. Since the wall of the aorta has no support on the right side, it widens in this direction The pulmonary stenosis is an independent anomaly and has the *same etiology* as pulmonary stenosis without ventricular septal defect Lev and Saphir postulated that transposition of the arterial trunks is due to an *abnormality* in the absorption of the bulbus, as claimed by *Keith* It is thus an abnormality in the execution of the second phase of the development of the heart Instead of the normal *torsion* of 150° occurring at the distal ostium and *the minimal* back torsion occurring at the proximal ostium, here *is an increased back torsion at the proximal* ostium. This eliminates the necessity of torsion at the distal ostium, which is either diminished or completely absent. The underlying abnormality in the proximal bulbar ostium, which permits the *increased back torsion*, is an abnormality in the bulboatrial spur area. The center of this area should constitute a fixed point in development about which the bulbus and atrial canal rotate. Where the intimacy between the bulbus and atrial canal is not established, the proximal end of the bulbus in the process of its absorption is capable of back torsion in the elimination of the twist of the bulbar ridges This produces various positions of the aorta and the pulmonary artery. Lev and Saphir (1945) *suggested an* alternate etiology for the *assumed* abnormal absorption of the bulbus. They suggested that an abnormality in the formation of ridge 3B, whereby it takes on the course of the reptilian ridge 4B or 3C, may be responsible both for the abnormal absorption of the bulbus and for the *unequal division* of the aorta and pulmonary artery and their coni.

A new approach to the problem was begun by Shaner (1949) He studied early malformed pig embryos which *still* retained embryonic landmarks *to find a clue* for malformations. *In abnormal pig embryos* with overriding aorta (*tetralogy of Fallot*), he found evidence of *abnormality* in the development and absorption of the bulbus, due to defective development of the endocardial cushions, especially the insufficient excavation of the anterior This prevents the proper migration of the aortic orifice to the *left* ventricle, thus producing an overriding *aorta*. The pulmonary artery *may* be compressed between the crista supraventricularis and the ventricular wall to produce pulmonary or conus stenosis Doerr applied this theory to overriding aorta in man.

Vossenaar, likewise, following the work of Keith, Lev and Saphir, and Shaner, considered tetralogy of Fallot an abnormality in the incorporation of the bulbus into the ventricles. This may be due to (1) insufficient development of a portion of the wall of the bulbus cordis, (2) insufficient or delayed excavation of the inferior side of the anterior endocardial cushion, (3) insu*fficient* or delayed reduction of the bulboatrial crest, or (4) insufficient development of the dextrodorsal bulbar cushion B and ridge 3B. De la Cruz and Pio da Rocha

CLOSURE OF THE DUCTUS ARTERIOSUS.[3] The method of normal closure of the ductus is not clearly understood. It is in some way or other related to the onset of respiration. The latter results in a fall in pulmonary resistance and an increase in pulmonary flow This is associated with an increase in left ventricular flow and in systemic pressure. Thus, blood is drawn away from the muscular ductus, which contracts and becomes nonfunctioning within minutes after birth. It becomes anatomically closed by 3 months of age.

Pathogenesis of Individual Abnormalities. Most abnormalities are best explained on the basis of an *arrest in embryologic development* or *abnormal embryologic development* Some abnormalities likewise may be considered as *secondary hemodynamic consequences* of other abnormalities In transposition of the arterial trunks, a phylogenetic variant may be invoked, acting during embryologic development.

TRANSPOSITION OF THE ARTERIAL TRUNKS The term "transposition" as used here means an abnormality in the position of the aorta and the pulmonary artery with respect to each other or with respect to the chambers from which they emerge Hence, this term includes overriding aorta, partial transposition, Taussig-Bing heart, and complete transposition In *overriding aorta*, the aorta emerges from both ventricles, while the pulmonary artery emerges from the right ventricle In *partial transposition*, both vessels emerge from the right ventricle In *overriding pulmonary artery*, the aorta emerges from the right, while the pulmonary artery emerges from both ventricles In *complete transposition*, the aorta emerges from the right, while the pulmonary artery emerges from the left ventricle

The embryogenesis of transposition complexes has intrigued embryologists, anatomists, and pathologists for many years Peacock and others, in *tetralogy of Fallot*, considered the stenosis (due to fetal endocarditis) to be primary The increased right ventricular pressure resulted in a defect of the ventricular septum and displaced the interventricular septum to the left. This forced the aorta to emerge from the right ventricle Meckel considered the septal defect to be primary. This causes the aorta of necessity to arise from both ventricles or the right ventricle. The flow of blood through the aorta results in a deviation of the stream from the pulmonary artery, and hence the stenosis. Rokitansky considered the stenosis and defect secondary to transposition and all types of transposition due to a common abnormality in the septum trunci. An overriding aorta is produced by a parallel deviation of the truncus septum to the left. This results in *pulmonary stenosis* Because of the inability of the ventricular septum to meet the misplaced bulbar septum, a defect in the former results The other types of transposition are produced by various degrees of abnormal rotation of the septum trunci, resulting in its abnormal relationship to the ventricular septum, thus placing either one or both vessels in the wrong ventricles. This fundamental work was enlarged upon with variation by succeeding authors. Keith suggested that transposition was due to the abnormal absorption of the bulbus into the ventricles. Normally, the aortic portion should atrophy, while the pulmonary portion expands In transposition, the reverse occurs, placing the aorta ventrally and into the right ventricle, with the pulmonary artery in the left

Spitzer (1923) evolved a phyloontogenetic theory of transposition based on his theory of the normal development of the heart. In his opinion, transposition of the arterial trunks is due to a phylogenetic abnormality reinforced by ontogenetic and hydrodynamic factors. In his view, in the mammalian heart, there are certain "atavic" structures, that is, structures similar to those found in the ancestral tree, but which are present only in rudimentary form in the mammalian heart These are (1) a remnant of the obliterated right ventricular aorta of the reptile and (2) the crista supraventricularis In transposition, Spitzer theorizes that there is an abnormality in ontogenesis which permits an arrest in development in the particular case at a lower phylogenetic level. This results in a reawakening and development of the atavic features present in the mammal and the coordination of these features with those already attained by the mammal

The reactions are set off by some unknown stimulus, resulting in a lack of the usual amount of mammalian torsion (*detorsion*) of the cardiac tube or the presence of the amount of torsion present in the ancestral reptilian

[3] See also Part 1, Chap 3 *Editor.*

tricle. In defects associated with tricuspid atresia or pulmonary stenosis with normal aortic root, the defects may be considered as secondary hemodynamic effects created by an increase in pressure on the left or right side, resulting in a lack of completion of the pars membranacea and the surrounding anterior and posterior parts of the ventricular septum.

In transposition complexes, the ventricular septal defects are due to the lack of formation of the proximal bulbar septum, which is a concomitant of malabsorption of the bulbus, reinforced by the above hemodynamic effects These effects may result in defective formation of the posterior ventricular septum as well, producing the large defects or complete absence of the ventricular septum

PULMONARY STENOSIS, ATRESIA, AND HYPOPLASIA The pulmonary hypoplasia, which is associated with transposition, may be explained by the uneven division of the bulbus during its malabsorption The true valvular stenosis of isolated *pulmonary stenosis* or *pulmonary stenosis* with defects, or that found in the uncommon case of tetralogy of Fallot, cannot be readily explained either as an inhibition or as an abnormal development Perhaps it can be explained as a secondary hemodynamic effect. It is here that fetal endocarditis still remains a possibility.

AORTIC STENOSIS OR ATRESIA In *supravalvular* aortic stenosis, there may be an exaggeration of the ridge formation normally found in the upper margins of the sinuses of Valsalva of the aorta Aortic stenosis, where the involvement is basically *in the valve*, is difficult to explain as an embryologic variant, and hemodynamic phenomena secondary to abnormal valve formation or a fetal endocarditis may be postulated In hypoplasia of the *aortic tract complex* with aortic stenosis or atresia, the latter may be considered secondary hemodynamic effects of decreased flow

TRUNCUS ARTERIOSUS COMMUNIS PERSISTENS In this anomaly, there is failure of development of the aortopulmonary septum, due to lack of formation and fusion of the spurs between the fourth and sixth arches This is usually associated with malabsorption of the bulbus, hence the origin of the truncus in a riding position or from the right ventricle

AORTOPULMONARY SEPTAL DEFECT Such a defect may be explained as an embryologic lack of fusion of the septum aorticopulmonale with the distal bulbar cushions 1 and 3

HYPOPLASIA OF THE AORTIC TRACT COMPLEXES. There are at least three possible embryologic variants in this group of anomalies: (1) There may be hypoplasia of the fourth left arch, with a corresponding unequal division of the truncus by the spurs between the fourth and sixth arches. (2) There may be a lessened flow of the inferior vena caval blood through the foramen ovale into the left side during embryologic life. In the latter case, there may be an abnormality in the approximation of the septum primum and secundum. (3) There may be an abnormally large ductus arteriosus, perhaps related to increased pulmonary resistance and lessened pulmonary flow. Thus, the left side is anatomically hypoplastic to a varying extent, and the right side is anatomically hyperplastic just before birth. This represents an exaggeration of the normal condition. Where the complex includes mitral atresia or stenosis, the latter may be considered to be hemodynamically produced because of lack of or altered flow.

COARCTATION OF THE AORTA. The *infantile (preductal)* and the *adult (postductal) types* apparently have a different genesis In the former, there is a hypoplasia of the fourth left arch, between the origin of the subclavian (or even more proximally) and the entry of the ductus arteriosus, which is always widely patent This segment in the fetus has less flow than the ascending or descending aorta. Thus, as in hypoplasia of the aortic tract complexes, the primary abnormality may be the hypoplasia of the fourth left arch, or the other factors mentioned in hypoplasia of the aortic tract

The pathogenesis of the adult (postductal) coarctation is unknown It is apparently related to the manner in which the ductus arteriosus enters the aorta and the manner of its partial or complete closure It is possible that fibrotic shortening and closure of the ductus exerts a pull and angulation upon the aorta or actually involves the latter in its fibrotic metamorphosis.

ABNORMAL AORTIC ARCHES AND BRACHIOCEPHALIC VESSELS. In *double aortic arch*, both fourth arches persist in their entirety, keeping their communication with the dorsal aorta. In a *right aortic arch with a left diverticulum*, the right fourth arch persists as the aorta, while the

thought that overriding aorta and all types of truncoconal anomalies are related to (1) delay in disappearance of the conoventricular flange (spur), (2) complete or incomplete lack of rotation of the truncoconal septum, (3) unequal partitioning of the truncoconus, (4) defects in growth of the truncoconal ridges, and (5) total or partial absence of the aortic and pulmonary semilunar primordia, fusion or increased number of primordia. Each or any combination of these may occur.

STENOSIS OF THE LOWER BULBAR ORIFICE. This anomaly may be considered as an abnormality in the final fusion of the conus of the pulmonary artery with the right ventricle after the absorption of the bulbus This may occur without an abnormality in the absorption of the bulbus (conus stenosis without transposition) or with such an abnormality (transposition with conus stenosis)

SUBAORTIC STENOSIS. Here we may postulate that the final absorption of the bulbus and fusion of the conus of the left ventricle with the left ventricle proper occurs poorly This may be considered a counterpart of stenosis of the lower bulbar orifice on the right side.

ATRIAL SEPTAL DEFECTS. *Patent Foramen Primum.* This represents the persistence of a fetal condition and may be ascribed to (1) a failure of upward extension of the fused endocardial cushions, (2) a failure of fusion of the dorsal and ventral endocardial cushions, or (3) an inhibition of growth of the septum primum.

Patent Foramen Ovale (Secundum Type) This anomaly, in the primary form, may be due to a greatly enlarged foramen ovale I or II or both, that is, a lack of growth and hence an overlapping of the septum primum and secundum. As a complication of other abnormalities, the *foramen ovale may remain patent because of increased pressure on the right or the left side of the atrial septum*

COMMON ATRIOVENTRICULAR ORIFICE. This represents a persistence of the fetal condition, brought about by a lack of fusion of the anterior and posterior endocardial cushions Because of this lack of fusion, endocardial material does not extend upward to close the foramen primum, and none descends to close the interventricular foramen

TRICUSPID AND MITRAL STENOSIS OR ATRESIA. These anomalies are due to an abnormality in the fusion of the anterior and posterior endocardial cushions and in the subsequent growth of the resultant mitral and tricuspid orifices In *tricuspid atresia* or *stenosis* without transposition, this orifice may be encroached upon as the atrial canal moves posteriorly and to the right, during the second phase of the development of the heart. The expansion and definitive position of this orifice is fundamentally dependent upon this movement. *Mitral stenosis* and *atresia* without transposition, however, are better explained as secondary anomalies due to altered hemodynamics, resulting in hypoplasia of the aortic tract complexes, as described below. In *complete transposition with tricuspid or mitral atresia,* there is a combined abnormality in the absorption of the bulbus and in the concomitant division of the atrial canal and its shift to the right and posteriorly behind the bulbus. The abnormally absorbed bulbus, with its resultant transposed vessels, may abut against the mitral and tricuspid orifices, producing a narrowing or atresia As the realignment of the bulbus and atrial canal may not occur at all, there may be a lack of fusion of the endocardial cushions, leaving a common AV orifice to one side of the transposed arteries (complete transposition with common AV orifice)

EBSTEIN'S ANOMALY. Two possibilities present themselves as embryologic variants in this anomaly (1) The right proximal bulbar cushion may join the fused endocardial cushions to form the lateral cushion as in the normal, but this cushion may hang down more distally than normal into the ventricle This gives rise to the displaced anterior and inferior leaflets (2) There may be greater than normal downward displacement of the cushion materials during their distal migration in the second phase of the development of the valves.

DEFECTS OF THE VENTRICULAR SEPTUM. In the usual isolated small septal defect (*maladie de Roger*), there is probably a lack of growth of the fused endocardial cushions, or perhaps the bulbar cushions, with resultant failure finally to close the interventricular foramen after the normal absorption of the bulbus (Fig 6-1). Thus, the defect is in the *pars membranacea* and between it and the anterior septum. In a *high septal defect,* there is defective formation of the bulbar septum. Hence, the defect opens into the conus of the right ven-

2

Pathology of congenital heart disease

MAURICE LEV

GENERAL CONSIDERATIONS

The pathology of congenital heart disease is best considered in relation to the myocardium and endocardium. Within the myocardium, *hypertrophy* or *atrophy* is the outstanding change seen. Occasionally, in isolated types of anomalies, *fibrosis* may be encountered. In the endocardium, only *endocardial hypertrophy* (*fibroelastosis*) and *sclerosis* will be discussed.

Hypertrophy of the myocardium is best described as that related to (1) contraction on an increased volume (which might be called volume hypertrophy), (2) contraction against increased [illegible]

be utilized in the discussion of pathogenesis of the complexes.

Congenital malformations of the heart have a tendency to be arranged in certain pathologic patterns or complexes (Lev, 1953). These are of two types: (1) a group of anomalies may be constantly found associated, and (2) a single anomaly may produce a constant pathologic picture. Our discussion of the pathology of congenital heart disease will thus be centered about the discussion of pathologic complexes, rather than on individual anomalies.

TRANSPOSITION COMPLEXES

Transposition of the great arterial trunks, according to Abbott, is that condition in which the great trunks have undergone an alteration in their relative positions to each other, or to the ventricles from which they emerge, whereby the aorta comes to lie in the path of the unaerated blood from the right ventricle (Abbott, 1927; Edwards, 1953; Rokitansky; Taussig, 1938).

Thus, this category of anomalies includes those conditions where the aorta *emerges from* both ventricles or from the right ventricle alone and the pulmonary artery springs from the right or left or both *ventricles*. Also included are those conditions of mutually abnormally situated arterial *vessels arising from* a common or slightly subdivided ventricle. Likewise, *conditions of* truncus communis, truncus solitarius aorticus and pulmonalis fall into this category, where the aortic vessel or *component* emerges from the *right or both ventricles*.

Thus, transposition of the arterial trunks, following and expanding Rokitansky's concepts, may best be classified as follows: (1) *overriding aorta*, (2) partial transposition, (3) *overriding pulmonary artery*, and (4) complete transposition. In *overriding aorta*, the aorta emerges from both ventricles, while the pulmonary artery emerges from the right. In *partial transposition*, both the aorta and the pulmonary artery emerge from the right ventricle. In *overriding pulmonary artery* (*Taussig-Bing heart*), the pulmonary artery arises from both ventricles, while the aorta emerges from the right ventricle. In *complete transposition*, the aorta emerges from the *right while* the pulmonary artery emerges from the left ventricle.

Thus transposition complexes in normal levocardia may be classified as shown below.

A. Overriding aorta
   1. With aneurysm of the pars membranacea
   2. With pulmonary tract hypoplasia (tetralogy of Fallot)

left fourth remains only in part as a diverticulum, giving off the subclavian In *right aortic arch with left descending aorta,* the right fourth arch persists and is pulled over by an aberrant left ductus or the left subclavian. Where the *right subclavian arises from the descending aorta,* there is persistence of the right dorsal aorta between the subclavian and common dorsal aorta, accompanied by an atrophy of its proximal portion. The various *anomalies of the left subclavian,* such as origin from the ductus, from the pulmonary, or from the aorta distal to the ductus, are related to various stages in arrest in the proximal migration of the subclavian

ORIGIN OF A CORONARY ARTERY FROM THE PULMONARY ARTERY. In this anomaly, one of two embryologic variants is possible. (1) Either the primordial thickenings of the coronary arteries are laid down on the wrong side of the junction of the aortopulmonary septum with the distal bulbar cushions, or (2) the septum meets these ridges in an aberrant manner.

PATENT DUCTUS ARTERIOSUS The pathogenesis of patent ductus arteriosus is unknown It may be related to abnormal angle of entry into the aorta, abnormal pulmonary factors initiated with respiration, or persistent large flow. The pulmonary factors may be purely anatomic or hemodynamic. Hemodynamic factors might be represented by too great a fall in pulmonary pressure upon initiation of respiration with resultant left-to-right flow through the ductus, or too small a fall, with persistent right-to-left shunt

LEFT SUPERIOR VENA CAVA This results from the retention of the communication of the left precardinal with the left common cardinal vein.

ENTRY OF THE PULMONARY VEINS INTO THE SYSTEMIC CIRCUIT. The following possibilities present themselves as embryologic variants in this anomaly: (1) The presplanchnic channels, instead of uniting with an outgrowth from the cardiac tube, effect a union with any of the following: (*a*) the precardinal veins (entry of the pulmonary veins into the right or left superior vena cava); (*b*) the post-, supra-, or subcardinal veins (entry into the inferior vena cava or azygos); (*c*) the vitelline-umbilical venous systems (entry into the portal vein); (*d*) the right horn of the sinus venosus (entry into the right atrium); or (*e*) the transverse horn of the sinus venosus (entry into the coronary sinus). (2) There may be an abnormality of the septum primum.

ABNORMAL RELATIONSHIP OF CARDIAC CHAMBERS. The pathogenesis of these abnormalities is not understood. In *mirror-image dextrocardia,* the AV loop curves in an opposite direction than normal. In *pivotal dextrocardia,* the normally formed AV loop is rotated in the horizontal plane to the right *Mixed dextro- and levocardia,* where the atria and ventricles do not correspond, has no ready explanation.

CONGENITAL ABNORMALITIES IN THE CONDUCTION SYSTEM The abnormalities in direction, such as in patent foramen primum, common AV orifice, ventricular septal defect, cor biatriatum triloculare, and cor triloculare biventriculosum, are related to a shift in direction posteriorly of the AV node, the AV bundle, or both, due to the defects. Abnormalities in continuity are usually related to fibrotic metamorphosis around the defects.

2

Pathology of congenital heart disease

MAURICE LEV

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Hypertrophy of the myocardium is best described as that related to (1) contraction on an increased volume (which might be called volume hypertrophy), (2) contraction against increased peripheral resistance (which might be called pressure hypertrophy), and (3) *ischemia* (ischemic hypertrophy) This terminology will be utilized in the discussion of pathogenesis of the complexes

Congenital malformations of the heart have a tendency to be arranged in certain pathologic patterns or complexes (Lev, 1953) These are of two types. (1) a group of anomalies may be constantly found associated, and (2) a single anomaly may produce a constant pathologic picture Our discussion of the pathology of congenital heart disease will thus be centered about the discussion of pathologic complexes, rather than on individual anomalies

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defect is usually situated in the basal part of the anterior portion of the ventricular septum and is of varying size It usually opens below the deviated crista into the right ventricle, but may pass through the crista. The pulmonary tract is narrowed in the region of the conus, in that of the pulmonic valve, or in both The *usual narrowing is in the conus* A contribution to this narrowing is the abnormality in the *crista supraventricularis*

In this anomaly, the septal band of the crista, which may be single or double, is hypertrophied The parietal band is deviated anteriorly, away

-d parietal

on

ng

of the conal tract. The septal and pari... ...ds may be divided by the defect, so that only a small band of muscle separates the aorta and pulmonary artery This conal narrowing may be further reinforced by *fibroelastosis.*

The right ventricle is hypertrophied, but is usually thinner than the left ventricle The left atrium and ventricle vary in size from normal to smaller than normal The tricuspid valve may show varying degrees of *mitralization*, that is, the medial leaflet may be connected to papillary muscles or may be fused with the anterior or the inferior leaflet The coronary ostia may be rotated in a counterclockwise manner, looking from the aorta downward into the ventricle. In some cases of tetralogy, the left ventricle is also hypertrophied. When associated with an atrial septal defect, the anomaly has been called a *pentalogy*

PATHOGENESIS OF THE COMPLEX The basic anomaly may be considered to be the overriding aorta and hypoplastic conus and pulmonary tree (see Chap 1) The ventricular septal defect may be explained on two bases (1) the abnormal absorption of the bulbus places the bulbar septum out of alignment with the main ventricular septum, (2) the closure of the ventricular septum occurs late in devel-

...d pulmonary

ventricular foramen to remain open. The deviation of the crista, if not explained by *Spitzer's theory*, may be related to the flow pattern set up by the ventricular septal defect The fi...

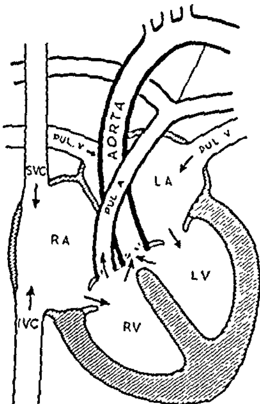


Fig 6-5. Diagrammatic sketch of blood flow in tetralogy of Fallot (From M. Lev Autopsy Diagnosis of Congenitally Malformed Hearts Charles C Thomas, 1953)

presents a "pressure hypertrophy" for this chamber contracts against the systemic resistance through the aorta and the increased pulmonary tract resistance Where the defect is large and the pulmonary stenosis *moderate* or mild, there may be *left-to-right shunt* through the defect (*acyanotic tetralogy*), and the right ventricle may have an increment of volume hypertrophy. It is in these cases, perhaps, that the left ventricle is also hypertrophied.

The blood flow in the usual case of tetralogy of Fallot is as follows (Fig 6-5). The *systemic* venous flow enters the right atrium and ventricle normally From the right ventricle, blood flows into the aorta and pulmonary artery. A decreased volume of aerated blood enters the left atrium and ventricle, and from there flows into the aorta.

Overriding Aorta with Aortic Hypoplasia (Eisenmenger's Complex). In this anomaly (Saphir and Lev, Selzer and Laqueur; Taussig and Semans), a straddling hypoplastic aorta



Fig. 6-3. Aneurysm of the pars membranacea Left ventricular view. (*From M. Lev Autopsy Diagnosis of Congenitally Malformed Hearts Charles C Thomas, 1953.*)

(*a*) With stenosis
(*b*) With atresia
3 With aortic hypoplasia (Eisenmenger's complex)
4. Common truncus in an overriding position
B Partial transposition
1. With pulmonary hypoplasia (Fallot type)
(*a*) With stenosis
(*b*) With atresia
2 With aortic hypoplasia (Eisenmenger type)
(*a*) Without mitral atresia
(*b*) With mitral atresia
3. Common truncus from right ventricle
C. Overriding pulmonary artery (Taussig-Bing)
D. Complete transposition

1. With normal architecture
2. With cor biatriatum triloculare
3. With single ventricle and small outlet chamber
4. With mitral or tricuspid atresia
5. Corrected transposition

Overriding Aorta with Aneurysm of the Pars Membranacea. In this anomaly (Lev and Saphir, 1937), the aorta straddles the muscular ventricular septum over an aneurysm of the *pars membranacea* (Fig. 6-3). The aorta emerges, however, only from the left ventricle, and hence, strictly speaking, this is not a transposition complex. The aneurysm bulges into the right atrium, right ventricle, or both The muscle bundles of the right ventricle may be normal, or the parietal band of the crista may be shortened and slightly deviated anteriorly and to the left, with an abrupt termination. The aneurysm may be associated with deformity of the aortic valve, with or without aortic regurgitation, or there may be secondary changes in the atrioventricular bundle with AV block, or there may be a secondarily produced ventricular septal defect The aneurysm may bulge into the tricuspid orifice, impeding its function.

Overriding Aorta with Pulmonary Tract Hypoplasia (Tetralogy of Fallot). In this anomaly (Rowe et al , Vossenaar), a large aorta straddles the interventricular septum over a defect of the latter, thus emerging to a varying extent from both ventricles (Fig 6-4). The





Fig. 6-4. Tetralogy of Fallot. A. Anterior view. B View looking into the ventricular septal defect from the right side. C, crista; D, defect; A, aorta; P, pulmonary artery.

A true Eisenmenger complex, from the pathologic standpoint, can be differentiated from ventricular septal defect by the abnormal architecture of the muscle bundles of the right ventricle However, a distinction must be made between the Eisenmenger syndrome, clinically, and the morphologic findings. Both an Eisenmenger complex and a ventricular septal defect, anatomically, may correspond to what clinicians consider an Eisenmenger syndrome (ventricular septal defect with right-to-left shunt), on the one hand, or a ventricular septal defect with the usual left-to-right shunt, on the other

PATHOGENESIS OF THE COMPLEX The overriding aorta may again be considered the primary anomaly and the ventricular septal defect as secondary Flow from the right atrium into the right ventricle is normal Flow from the right ventricle at birth, and in the young, is probably completely into the pulmonary artery, although there is probably some increase in pulmonary resistance Increased pulmonary flow proceeds into the left atrium and ventricle Flow from the left ventricle passes both into the aorta and into the right ventricle Thus, the right ventricle presents both a pressure and a volume hypertrophy The left atrium is enlarged because of increased flow, while the left ventricle may be normal in size or enlarged, because of increased flow and decreased pressure factors With increasing age, the pulmonary resistance is known to increase and with it the pressure factor in the right ventricle, accompanied by decreased pulmonary flow

Common Truncus in an Overriding Position. In this anomaly (Collett and Edwards, Humphreys et al , Kreutzer et al), only one artery emerges from the heart, giving rise to the coronary, pulmonary, and systemic arteries. This anomaly must be differentiated from a *truncus solitarius aorticus* or *pulmonalis*, where a band (or minute blind artery representing the aorta or pulmonary artery) may be found The common truncus straddles the ventricular septum over a defect of the latter. The right ventricle is hypertrophied, while the left ventricle may be hypertrophied, normal, or small The architecture of the muscle bundles of the right ventricle, the defect of the ventricular septum, and the position of the coronary arteries are typical of overriding aorta The pulmonary trunk may come off beneath a partial septum, or the two pulmonary arteries of varying size may come directly from the aorta.

PATHOGENESIS OF THE COMPLEX. The common truncus may be considered as the primary abnormality, with the ventricular septal defect secondary (see Chap. 1). The right ventricle presents a pressure hypertrophy, since it is related to an increased pulmonary resistance. Blood from the left and right ventricles enters the common truncus and is distributed to the systemic and pulmonary circuits in different amounts, depending upon the size and position of the pulmonary arteries. Where there is a partial pulmonary trunk, there is increased flow (as in Eisenmenger's complex), and the left atrium is therefore hypertrophied and the left ventricle may be normal or large, depending upon the opposite effects of increased flow and decreased peripheral resistance (Eisenmenger type of common truncus) Where the pulmonary arteries come off directly from the truncus, more or less at right angles if they are of considerable size, the pulmonary flow may be normal but not increased. When the pulmonary arteries are small, then the flow is decreased Under these circumstances, the left atrium is normal or small and the left ventricle is smaller than normal, resembling tetralogy of Fallot (Fallot type of common truncus).

Partial Transposition with Pulmonary Hypoplasia (Fallot Type). In this anomaly (Lev, 1953), a large aorta comes off almost completely from the right ventricle, in addition to the small pulmonary artery (Fig 6-8B) The defect of the ventricular septum is the same as in tetralogy of Fallot or larger The right ventricle is markedly hypertrophied, while the left atrium and ventricle are small. The coronary ostia are still more rotated in a counterclockwise direction than in tetralogy of Fallot The architecture of the muscle bundles is somewhat d[illegible]

[illegible] band, which forms the crista, is still further deviated over the anterior wall of the right ventricle away from the anterior leaflet of the tricuspid. The crista so formed lies distal to, as well as above, the ventricular septal defect, which is bounded by the parietal band and an accessory small septal band lying posterior to the defect An accessory parietal band

rides over the ventricular septum over a defect of the latter, emerging to a varying extent from both ventricles (Fig. 6-6A) The pulmonary artery is normal in size or enlarged. The defect is the same as that seen in tetralogy of Fallot. The right ventricle is again hypertrophied, but the left atrium and ventricle are larger than in Fallot. The aortic valve may be deformed, with or without aortic insufficiency. The pulmonary valve ring may be sufficiently dilated to produce relative pulmonary insufficiency. The coronary ostia may be rotated as in Fallot The architecture of the muscle bundles of the right ventricle may resemble that in Fallot, but frequently the parietal muscle bundle is enlarged rather than shortened.

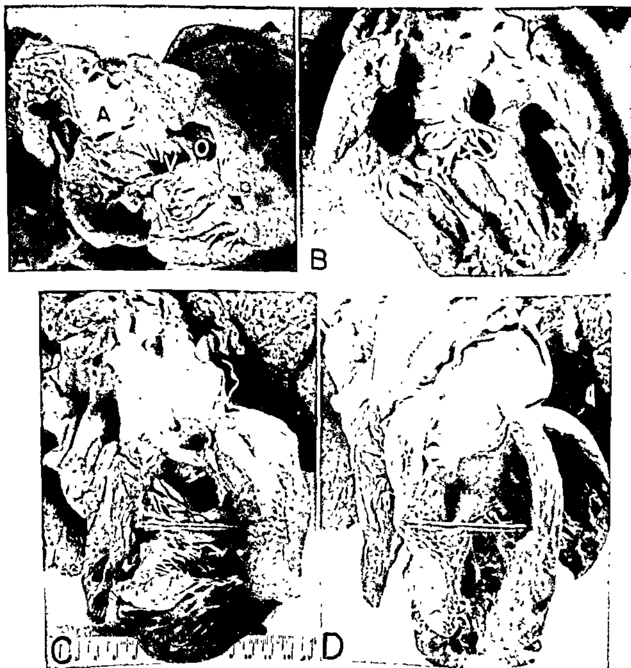


Fig 6-6. A The Eisenmenger complex Right ventricular view, looking into the aorta A, aorta, V, ventricular septal defect, O, outflow tract of pulmonary artery B Partial transposition, Fallot type, right ventricular view, looking into the aorta C Partial transposition, Eisenmenger type Right ventricular view, looking into the aorta D. Partial transposition, Eisenmenger type Right ventricular view, looking into the pulmonary artery. (*From M. Lev. Autopsy Diagnosis of Congenitally Malformed Hearts Charles C Thomas, 1953.*)

Etiology. SA block is observed as a normal finding in individuals presenting an increased vagal tone. By itself, it is not considered abnormal. It may be produced in a susceptible individual by carotid sinus pressure. It is also observed in infectious states, during acute rheumatic carditis, in the presence of arteriosclerotic processes involving the SA node, and as a result of digitalis. Quinidine, procaine amide, and hyperpotassemia may also produce this condition; however, these drugs tend to depress atrial contraction relatively early without concomitant effects on the ventricles; thus, they produce AV dissociation and ultimately sinus arrest with the maintenance of ventricular beats.

Pathology. No characteristic pathologic findings are observed in SA block. It may occur in patients with disease of the SA node due to rheumatic carditis or degenerative conditions, it may follow occlusion of the right coronary artery, which supplies the SA node in 60 per cent of hearts. Occasionally, an arteriosclerotic process present in the region of the carotid sinus may tend to produce SA block by its increase of vagal tone.

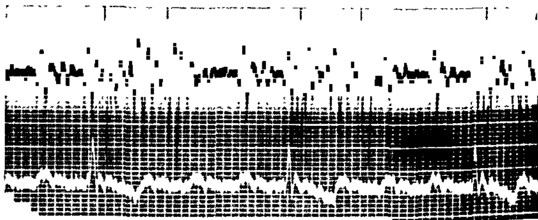
Symptoms. No symptoms are usually observed with SA block. This arrhythmia may, however, produce symptoms under the following circumstances. Occasionally, the period of block may be prolonged to several seconds, resulting in syncopal attacks However, the periods of cardiac standstill are frequently shortened by the temporary assumption of the role of pacemaker by the AV node (*nodal escape*) or by a ventricular focus (*ventricular escape*). Such episodes may result in a sensation of palpitation or forceful beating of the



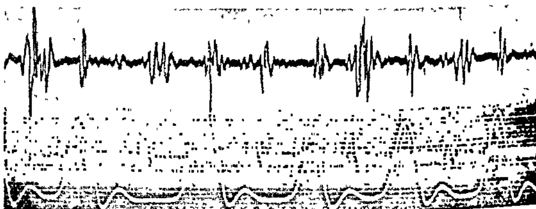
Fig. 11-16. A Partial AV block. Initial strip shows prolongation of the P-R interval, which measures 0.22 sec. Second strip. note the P-R interval prolongation with the tachycardia (ventricular rate, 150 per minute). Note that the P wave of the prolonged P-R interval immediately follows the preceding QRS complex, coming between the QRS complex and the T wave. This P wave controls the following QRS complex. B Partial AV block. Progressive increase in the prolongation of the P-R interval until a dropped ventricular beat is observed at P_X (Wenckebach phenomenon). C. Complete AV block. The atrial rate is 100, the ventricular rate is 37 per minute. Each pacemaker is beating independently of the other. D. Complete AV block with ventricular extrasystoles, some of which appear in groups of two in succession Note the regular atrial rate of 88 per minute and a regular but slow ventricular rate (16 per minute) in most cycles, the two rhythms are entirely independent of each other.



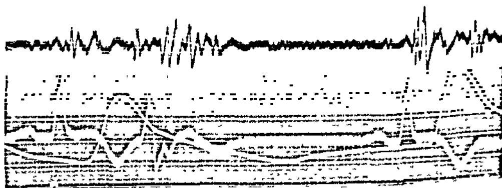
A



B



C



D

Fig. 11-19. A. Supraventricular tachycardia. Phonocardiogram (stethoscopic) 2R2. B. Atrial flutter. Phonocardiogram (stethoscopic) 2R2. C. Atrial fibrillation. Phonocardiogram (stethoscopic) 5L7-O S. D. Ventricular extrasystole. Phonocardiogram (stethoscopic) 4R2 Od.

should lead one to suspect the diagnosis (see Chap. 7).

In partial block (2:1), exercise or amyl nitrite may abruptly double the ventricular *rate*. When the apical rate is regular and ranges *from* 20 to 40 per minute and is relatively unaffected by exercise or atropine, complete AV block should be suspected *The 1st heart sound* [illegible]

relatively loud, when *they are far apart*, the 1st sound is faint (see also Chap. 8). The independent movements of *the atria* are usually visible upon a fluorescent screen.

The auscultatory phenomena in AV block should be differentiated from premature systoles, SA block, sinus arrhythmia, sinus bradycardia, and AV *nodal* rhythm. A 3:2 AV block may *simulate* a bigeminal rhythm The diagnosis is clearly established by the electrocardiogram

ELECTROCARDIOGRAM. Partial AV block is recognized easily by the electrocardiogram, which clearly shows regularly recurring, normally shaped P waves with prolonged P-R intervals (Fig 11-16) The P-R interval is prolonged to over 0 21 sec in adults and over 0 18 sec in children With a higher grade of partial block, dropped beats may be detected However, prolongation of the P-R interval or nonconducted atrial impulses of other etiologies must be excluded. Thus, in atrial premature systoles and in the atrial beat occurring at the time of the nodal escape, prolonged P-R intervals, nonconducted atrial impulses, or both, may be observed AV *dissociation and interference* dissociation may also be associated with P-R interval prolongation not due to partial AV block (see Chap 11) In all these instances, the atrial impulse reaches the AV junctional tissue during its normal relative or absolute refractory phase In AV block, on the other hand, the cause for the disturbance resides in a depression of the AV junctional tissue

Complete Atrioventricular Block. In complete AV block, the atria beat regularly at a rate of 70 to 80 per minute in response to their pacemaker, the SA node, and the ventricles also beat regularly at a rate of 20 to 40 per minute in response to their center located in the lower portion of the AV node, in the bundle of His, or in the upper *portion* of the interventricular septum. *These two pacemakers function entirely independently of each other.* The atrial rate is influenced by the vagus and by factors which influence sympathetic *tone.* With normal sinus rhythm, the ventricular rate is controlled entirely by *the events* occurring in the atria In complete AV block, this situation no longer holds true since the ventricles presumably have no vagal innervation, therefore, they usually are not influenced by changes in vagal tone. The ventricular rate, however, can vary to some slight degree, being modified by factors that alter sympathetic tone, such as *fever and the injection* of *epinephrine* or other sympathomimetic drugs. If the idioventricular pacemaker is located in the lower portion of *the AV node, terminal* fibers of the vagus may partially control it. In such cases, a large dose of atropine may slightly increase the ventricular rate

ELECTROCARDIOGRAM. The electrocardiographic diagnosis is easily made (Fig 11-16). The ventricular complexes occur regularly and slowly. While the ventricular rate is usually slow, 30 to 40 per minute, it may be higher (60 per minute) in complete heart block due to digitalis, in the cycles immediately following emergence from Stokes-Adams seizures, it may be 100 per minute The atrial complexes usually occur regularly at a normal rate. Occasionally, the atrial rate is quite rapid, 110 to 150 per minute; rarely it is slow, below 40 per minute. Occasionally, *sequences are observed* where two atrial beats are followed by one ventricular complex, thus resembling a 2:1 heart block *The Stokes-Adams syndrome* is characterized by syncopal attacks, convulsions, or epileptiform seizures, and occurs when there is a period of anoxia lasting over 3 to 9 sec. These episodes are the chief hazard and usual cause of death in patients with complete AV heart block. The following are the underlying mechanisms recorded electrocardiographically during the seizures (Fig. 11-17): (1) a prefibrillatory type of ventricular tachycardia (ventricular flutter), (2) ventricular fibrillation, (3) standstill *of the* whole heart, (4) ventricular standstill with maintenance of atrial beating These mechanisms may *occur either singly* or *in* various combinations.

TREATMENT. *Complete Atrioventricular Heart Block* No specific therapy is indicated

and murmurs may disappear if present, or, on the contrary, may appear during the attack.

2 *Posttachycardial syndrome.* Decreased loudness of the cardiac sounds, murmurs due to relative valvular insufficiency, and triple rhythm are frequent Following ventricular tachycardia, one can see a marked decrease in amplitude of the 1st sound, a systolic murmur in decrescendo, and a triple rhythm (summation type) The last two had disappeared during the attack but were previously present

NODAL RHYTHM

The changed time relationships between atrial and ventricular systoles cause marked changes of the phonocardiogram If present, an atrial *4th sound* disappears. The vibrations of the 1st sound, owing to closure of the AV valves, have an amplitude which varies in proportion to the P-R interval This is because of different tension of these valves at the beginning of systole In nodal rhythm, the 1st sounds have constant loudness, while in cases of wandering pacemaker, there are continuous changes A short systolic sound due to atrial contraction may appear

SINOATRIAL BLOCK

There are only two published phonocardiograms in cases with bigeminal SA block The cardiac sounds either remain unchanged, or they alternate in amplitude, number of vibrations, and duration (Fig. 11-21A)

ATRIOVENTRICULAR BLOCK

Complete Atrioventricular Block without Valvular Lesions. *Atrial sounds* are present both in systole and diastole (Fig. 11-21B). In esophageal phonocardiograms and, occasionally, in precordial tracings, they present *three groups of low-pitched vibrations:* the first is caused by the atrial contraction, the second seems to be due to the resulting ventricular distention or a vibration of the AV valves, the third, to an elastic recoil of the ventricular walls In precordial tracings, where the three groups are recorded, they occur 0 04, 0 12, and 0 27 sec after the respective P wave, and the duration of the atrial sound complex is from 0 34 to 0 36 sec However, the first group of vibrations is seldom recorded. Then the atrial sound complex starts 0 06 to 0 12 sec after the P wave and lasts from 0.15 to 0 22 sec The atrial sounds during systole consist of one or two groups of vibrations, and they can be larger than the diastolic Their mechanism of production is still discussed. Some authors feel that these sounds are directly caused by atrial contraction which causes a vibration of the closed AV valves. *Atrial murmurs* can be seen in diastole in older patients 0 14 to 0.23 sec after the beginning of the P wave. These murmurs, occurring *after* atrial contraction, can be explained by sclerosis of the AV valves, which at first hinders their upward movement, causing a moderate regurgitation, and then delays their opening, thus slowing the normal

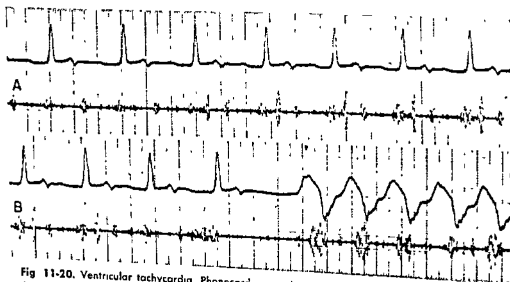


Fig 11-20. Ventricular tachycardia Phonocardiogram (stethoscopic) 3M. (0.02 in and 0 10 in). A and B are consecutive sections of the same tracing.

posite directions, giving rise to the isoelectric or transitional P wave. Such beats are said to be *fusion beats.*

ATRIOVENTRICULAR BLOCK

Partial Atrioventricular Block. Atrioventricular (AV) block may be divided into two types: partial, or incomplete, and complete. AV block may be *temporary, intermittent,* or *permanent,* and one type may develop into the other. The first stage of AV heart block is said to occur when the AV conduction time (P-R interval) exceeds 0.20 sec As the degree of block increases, the AV conduction time becomes longer and longer until dropped beats occur, i e., the ventricles fail to respond to some atrial beats. In a still higher grade of block, there may be observed 2:1, 3:1, or an even higher degree of partial AV block As the block further increases, a stage is reached in which the ventricles fail to respond to *any* atrial impulse, with the result that ventricles and atria beat entirely independently of each other When this stage is reached, the degree of AV block is said to be *complete*

Sudden death may occur during the transition from partial to complete block because of ventricular standstill or ventricular fibrillation.

Clinical heart block has been observed as the result of the following. (1) infections, (2) certain drugs, especially digitalis and, to a lesser degree, quinidine and Pronestyl; (3) congenital cardiac anomalies, (4) vagal stimulation; (5) degenerative conditions; and (6) hypoxia. A discussion of these conditions follows

PATHOLOGY. Coronary artery disease, acute or chronic, is the most common cause of AV block in the older age group. The right coronary artery supplies the AV node in 92 per cent of hearts, the left coronary in 8 per cent Gummata occurring in the AV node or bundle of His are rare (see also Chap. 5)

SYMPTOMS AND SIGNS In partial AV block, no symptoms due to the block itself may be observed, even with a slow ventricular rate The symptoms are those of the underlying disease. Some patients with complete AV block present no symptoms, usually, however, they complain of fatigue on exertion, occasional precordial pain, and consciousness of a vigorous, slow, forceful heart action. These patients usually cannot engage in strenuous physical exertion but generally do fairly well on a reduced physical regimen.

As a result of the slow rate, alterations in the cardiovascular dynamics appear. The cardiac output per beat is increased, but the cardiac output per minute, as compared to the normal, may be decreased in some patients. In complete AV block, because of the fixed cardiac rate, the mechanism for increasing cardiac output in response to exertion and excitement is seriously impaired. Exertion may lead to the production of an extrasystolic arrhythmia and, if continued, may precipitate a Stokes-Adams attack. The systolic blood pressure is elevated, rising to about 170 to 200 mm; the diastolic pressure is usually low, 80 to 100 mm. It is distinguished from true hypertension by the relatively low diastolic pressure resulting from the longer emptying time available to the large arteries between heart beats. The systolic pressure rise is evidence of the enhanced vigor of the slow beats resulting from the greater filling time allowed the heart. The heart, particularly the left ventricle, is enlarged

The important symptoms to be considered in the higher grades of partial and complete AV heart block are the development of *giddiness, fainting,* and *temporary loss of consciousness, with or without convulsive seizures (Stokes-Adams syndrome).* These manifestations of cerebral hypoxia occur during the transition from partial to complete AV heart block, as well as during the course of complete cessation of cerebral flow for 3 to 9 sec or longer.

DIAGNOSIS. The possibility of AV block should be suspected in the presence of any of the conditions mentioned above, especially rheumatic fever, coronary diseases, digitalis, toxic factors, etc. Suggestive evidence consists in a *diminished intensity of the 1st heart sound,* which may be marked. In the presence of dropped beats, the auscultatory phenomena closely resemble and should be differentiated from extrasystoles with a compensatory pause. When there is a delay in AV conduction (prolonged P-R interval) with a regular rhythm ranging from 50 to 80 per minute, the diagnosis is practically impossible by auscultation alone. With rates below 50 or 40 per minute, the possibility of partial or complete heart block should be considered. The presence of a jugular pulse more rapid than that of the apex

sound, on account of the variable duration of diastole.

Cases with Mitral Lesions. Frequently the sclerosis of the mitral cusps increases the loudness of the 1st sound and causes its splitting. The Q-1st sound interval, which is particularly prolonged in mitral stenosis, becomes even longer if there is atrial fibrillation. This interval is inversely proportional to the duration of the preceding cardiac cycle: shorter diastole = longer interval (Luisada, Cossio). The *opening snap* of the mitral valve has duration and intensity which vary for every cycle (Rappaport and Sprague; Wells). This snap is more distant from the 2d sound when left atrial pressure is lower; therefore, it is more distant after a long diastole. *Murmurs* of mitral origin are known to disappear when atrial fibrillation starts. This is particularly true for the presystolic murmur, while the systolic and the mid-diastolic murmurs may disappear for a time and reappear later. On the other hand, the mid-diastolic murmurs of mitral stenosis may be louder than in cases with sinus rhythm. This may be explained by the fact that left atrial pressure is higher. A *ventricular type* of triple rhythm is frequent in mitral insufficiency, occasionally present in moderate mitral stenosis, and absent in severe mitral stenosis. It may simulate an opening snap

EXTRASYSTOLES

Extrasystoles (Fig. 11-19D) are characterized by the premature appearance, and possibly by the occasional absence, of cardiac sounds and murmurs Other possible signs are due to the extrasystole itself. Others may affect the preceding cycle (preextrasystolic signs) and some of the following beats

The 1st sound is usually accentuated and delayed, the Q-1st sound interval being from 0 08 to 0 10 sec and even 0.12 sec The main vibrations may be from two to four times higher than those of the normal contractions Sometimes the 1st sound is decreased and may be completely absent, it may be either shortened or prolonged, it may be split, but this is seen only in ventricular extrasystoles, on account of marked asynchronism of closure of the mitral and tricuspid valves.

Ventricular systole is usually short The *2d sound is usually small* and may become so faint as to disappear. This is more frequent in cases of early extrasystoles, especially if they are interpolated. Absence of both sounds is extremely rare; in such cases, *the extrasystole is clinically mute.* Because of asynchronism of the closure of the semilunar valves, *splitting* of the 2d sound may occur in ventricular extrasystoles. On the other hand, previous splitting of the 2d sound may disappear during the extrasystole.

Triple Rhythms. The atrial type disappears in ventricular extrasystoles because of the absence of atrial contractions. On the other hand, following an extrasystole, a ventricular type of triple rhythm may occur, or it may disappear if it was regularly present in the normal cycles. A summation type of triple rhythm may be seen in atrial or sinus premature contractions It is due to coincidence of the rapid filling of the preceding beat with the following atrial contraction. Extrasystoles may either increase or decrease the loudness of *murmurs* The latter may even disappear during an extrasystole because of inadequate filling of the ventricles

The extrasystoles may modify some of the graphic characteristics of the preceding cardiac cycle For instance, when they occur very early, the 1st sound may coincide with a 3d sound, and even with the 2d sound of the previous cycle This may cause increased loudness of that 2d sound, a summation type of triple rhythm, or an accentuation of the early-diastolic murmur of mitral stenosis. On the other hand, this murmur may disappear if several premature contractions occur in a row.

The 1st sound is frequently increased in the beat immediately following the extrasystole and, at times, in the second or third subsequent beat. Occasionally, *alternans* develops.

VENTRICULAR TACHYCARDIA

The phonocardiographic signs of the ventricular tachycardias are similar to those of the supraventricular forms.

1. *The attack.* During the attack, ventricles and atria beat independently and, now and then, contract at the same time. The 1st sound presents characteristic changes consisting of occasional sudden increase of loudness (Fig 11-20). The 1st sound may be prolonged or split, either constantly or intermittently, and is usually delayed. The 2d sound occurs early (short systole). Diastole is even shorter. As in supraventricular tachycardia, triple rhythms

1 to 2 hr, depending on desired results, or may be given as a 1:1,000 solution in oil (1.0 ml intramuscularly).

3. *Isuprel* may be given sublingually in doses of 10 to 20 mg every 2 hr or as required, subcutaneously 0.2 mg every 6 hr or as indicated, or intravenously as a continuous infusion of 1 mg Isuprel dissolved in 200 ml of 5 per cent glucose in distilled water, or 4 μg per ml, at a rate of 9 to 20 drops per minute.

4. Molar sodium lactate is effective when given promptly, preferably within 1 to 2 min after the onset of the attack. Initially, it should be given intravenously by syringe in doses of 20 to 40 ml in 1 to 2 min during the attack; then, the solution should be administered as an intravenous infusion at the rate of 60 to 150 drops per minute, the exact rate and amount depending on the effects observed. As the ventricular rate increases, the infusion should be slowed; when it becomes apparent that the pacemaker is spontaneously maintaining a satisfactory rate and the episodes of cardiac arrest have been eliminated, the infusion should be stopped.

5. An *artificial pacemaker* will restore cardiac beating during cardiac arrest. Its use may be lifesaving (see Chap. 12).

6. Because these seizures are so often repeated, thoracotomy accompanied by cardiac massage should be used only when all other methods fail.

7. *Barium chloride* increases the rhythmicity of the cardiac pacemaker but is not frequently used because of its toxic effects.

8. Quinidine and procaine amide have been used in the past when the Stokes-Adams seizures were associated with ventricular extrasystoles, ventricular tachycardia, or ventricular flutter. The administration of these drugs is considered to be contraindicated because they depress cardiac pacemakers.

9. Digitalis in the presence of congestive failure should be used with caution because of its effect in increasing cardiac irritability. AV block, if complete, is not a contraindication to the use of digitalis. Incomplete AV block, on the other hand, might be transformed into complete block by digitalis.

10. Defibrillation may be accomplished by application of the *defibrillator* (see Chap. 12) to the closed chest or after thoracotomy to the exposed heart.

and murmurs may disappear if present, or, on the contrary, may appear during the attack.

2 *Posttachycardial syndrome.* Decreased loudness of the cardiac sounds, murmurs due to relative valvular insufficiency, and triple rhythm are frequent. Following ventricular tachycardia, one can see a marked decrease in amplitude of the 1st sound, a systolic murmur in decrescendo, and a triple rhythm (summation type). The last two had disappeared during the attack but were previously present.

NODAL RHYTHM

The changed time relationships between atrial and ventricular systoles cause marked changes of the phonocardiogram. If present, an atrial *4th sound* disappears. The vibrations of the 1st sound, owing to closure of the AV valves, have an amplitude which varies in *proportion to the P-R interval. This is because* of different tension of these valves at the beginning of systole. In nodal rhythm, the 1st sounds have constant loudness, while in cases of wandering pacemaker, there are continuous changes. A short systolic sound due to atrial contraction may appear.

SINOATRIAL BLOCK

There are only two published phonocardiograms in cases with bigeminal SA block. The cardiac sounds either remain unchanged, or they alternate in amplitude, number of vibrations, and *duration* (Fig. 11-21A).

ATRIOVENTRICULAR BLOCK

Complete Atrioventricular Block without Valvular Lesions. *Atrial sounds* are present both *in systole and diastole* (Fig. 11-21B). In esophageal phonocardiograms and, occasionally, in precordial tracings, they present *three groups of low-pitched vibrations:* the first is caused by the atrial contraction, the second seems to be due to the resulting ventricular distention or a vibration of the AV valves, the third, to an elastic recoil of the ventricular walls. In precordial tracings, where the three groups are recorded, they occur 0.04, 0.12, and 0.27 sec after the respective P wave, and the duration of the atrial sound complex is from 0.34 to 0.36 sec. However, the first group of vibrations is seldom recorded. Then the atrial sound complex starts 0.06 to 0.12 sec after the P wave and lasts from 0.15 to 0.22 sec. *The atrial sounds during systole* consist of one or two groups of vibrations, and they can be larger than the diastolic. Their mechanism of *production is still discussed. Some authors* feel that these sounds are directly caused by atrial contraction which causes a vibration of the closed AV valves. *Atrial murmurs* can be seen in diastole in older patients 0.14 to 0.23 sec after the beginning of the P wave. These murmurs, occurring *after* atrial contraction, can be explained by sclerosis of the AV valves, which at first hinders their upward movement, causing a moderate regurgitation, and then delays their opening, thus slowing the normal

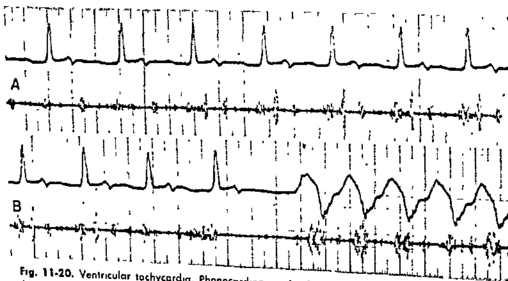


Fig. 11-20. Ventricular tachycardia. Phonocardiogram (stethoscopic) 3M. (0.02 in. and 0.10 in.). A and B are *consecutive* sections of the same tracing.

for the *asymptomatic* type of AV block; these patients do fairly well with a slow rate, which may range from 30 to 40 per minute. In the *symptomatic* type of AV block, in which the patient experiences frequent fainting episodes, administration of one or more of the following drugs is indicated: (1) sympathomimetic drugs (ephedrine, Isuprel), (2) oral molar sodium lactate.

Stokes-Adams Seizures. Prophylaxis consists of avoiding those factors which tend to precipitate attacks; e.g., strenuous exertion and emotional upsets. Between attacks, measures as described for AV block may be used. The active measures during an attack consist of the following:

1. Direct vigorous thumping on the precordium.

2. *Epinephrine* by intracardiac injection (0.25 to 1 ml of a 1:1,000 solution). This may also be given by slow-drip intravenously, *but not more than 0.25 mg should be given* by this route, and the drug must be administered at a very slow rate. To prevent repeated attacks, epinephrine may be given in doses of 0.2 to 0.3 ml subcutaneously every

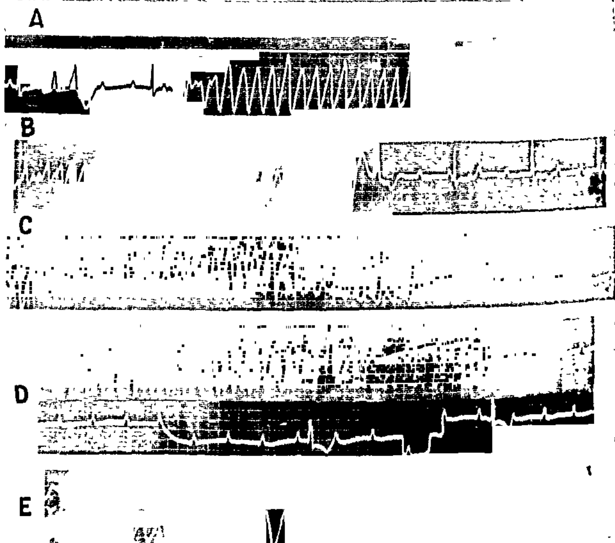
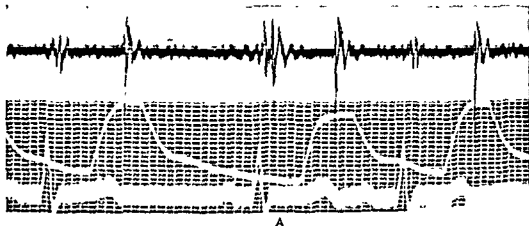


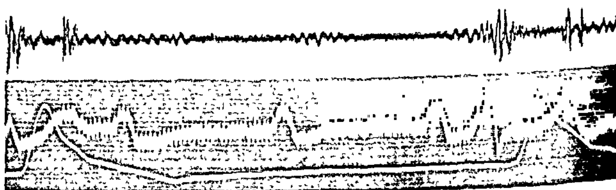
Fig. 11-17. Cardiac mechanisms during a Stokes-Adams attack. Strips A, B, C, D, and E are taken from the same patient, who had a complete AV block. A. Paroxysm of *ventricular flutter* with a ventricular rate which averages about 200 per minute. Note the markedly aberrant type of ventricular complexes. The end of the strip shows the resumption of the complete AV heart block. B. Ventricular flutter with a rate of about 200 per minute, terminating in ventricular standstill. The atrial rate is maintained at 100 per minute. C. Emergence from an attack of *ventricular standstill,* with the appearance of occasional idioventricular beats. D, and E. Ventricular *fibrillation.* Note the markedly aberrant type of ventricular response. The patient recovered from this paroxysm but succumbed during a subsequent attack.

ventricular filling. In other words, slight insufficiency and stenosis would take place in turn, both of them functional and of short duration.

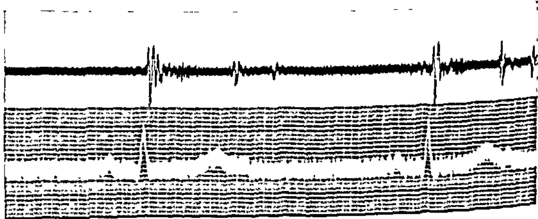
FIRST SOUND. *Splitting* of the 1st sound has been described. It is due to two separate groups of ventricular vibrations. Splitting may be simulated by presystolic or systolic occurrence of an atrial sound. *Changes in amplitude of the 1st sound* are also typical of complete AV block. In long tracings, one can see marked changes in amplitude from one beat to the next. The 1st sound may disappear almost completely, or it may increase in amplitude up to five or six times (*cannon sound*). The frequency, duration, and number of vibrations of the 1st sound usually follow the changes in amplitude. Thus, an increased 1st sound has a higher pitch and more vibrations. A definite relationship has been found between the amplitude of the 1st sound and the duration of



A



B



C

Fig. 11-21. A. Sinus bigeminy. B Complete AV block C. Incomplete AV block with Wenckebach periods. All phonocardiograms (stethoscopic) 5L6

arteries nearer the heart but not in those more distant When failure is severe, a high pulse wave may be followed by gradually smaller ones (*Galenus's pulse*).

As long as the conditions of the myocardium are good, the stroke *volume* is directly proportional to the length of the preceding diastole and inversely proportional to the stroke volume of the preceding cycle. (This, however, is approximate and not exact.) If there is cardiac failure, no rule can be established The *speed* of the small pulse waves is always greater than that of the large waves

Electrokymogram. This tracing has been studied by Lewis and Terry, Boone et al., and Engstroem et al The atrial tracing shows the absence of atrial waves The waves of the ventricular and arterial tracings (both the aortic and the pulmonic) have a variable amplitude, which is roughly proportional to the length of the previous diastole

PREMATURE BEATS

Jugular Tracing *Atrial premature beats* have A, C, and V waves which are similar to those of a normal tracing *Nodal* and *ventricular premature beats,* on the other hand, frequently have a high A wave, because of simultaneous atrial and ventricular contraction which is accompanied by a venous regurgitant wave

A *left ventricular premature beat* may show a delay of V over the 2d aortic sound (early contraction of the left ventricle, later contraction of the right, with late opening of the tricuspid valve).

Arterial Tracing, Hemodynamics. The pulse wave of the premature beat may be as high as a normal wave and occasionally higher *It is usually smaller and may be absent* on account of small ejection or even lack of ejection. Records taken over different arteries *show that* the pulse wave of the *premature* beat may be present in the arteries near the heart (carotid) and absent in those distant (tibial arteries) A drop in pressure occurs during the compensatory pause The following wave is higher than normal, and is followed by a smaller wave; this may start a *pulsus alternans*

The pulse of the premature contraction has a low systolic and a high diastolic pressure, while the following pulse is much larger, having a high systolic and a low diastolic pressure.

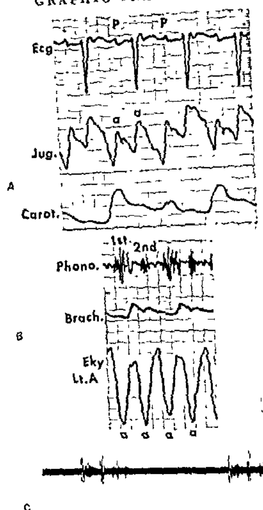


Fig. 11-18. Tracings revealing a greater number of atrial waves than ventricular waves. A. Multiple waves of atrial origin in the jugular tracing of a patient with atrial flutter B Multiple waves in the left atrial border electrokymogram of a patient with atrial flutter. C Multiple waves in the right atrial border electrokymogram in a patient with complete AV block Above, phonocardiogram; below, EKy.

From *two to three* pulse waves are necessary for reaching again a normal and stable level of blood *pressure.* On the other hand, the first normal contraction following *an interpolated premature beat* frequently yields a smaller pulse wave in the peripheral arteries (a short *diastole* precedes such an extrasystole).

The pulse wave of a *right* ventricular premature beat *may* be delayed over the beginning of the corresponding *1st apical* sound

the P-R *interval* For P-R intervals from 0 50 to 0 32 *sec*, the amplitude of the 1st sound is somewhat *increased*, from 0 32 to 0.23 sec, the amplitude is *decreased;* from 0 25 to 0.12 sec, it is moderately increased, from 0 14 to 0 04 sec, it is again *markedly increased* (cannon sound). When the P wave follows the R wave and there is an R-P interval of from 0 04 to 0 28 sec, the sound is *just slightly increased*

A *dissociated cannon sound* and a *double cannon sound* were described in cases of complete AV block with bundle branch block. The former is due to accentuation of *one* of the two components of a split 1st sound, the latter to accentuation of both components The variable amplitude of the 1st *sound has been* explained by the different position of the AV valves at the beginning of the systole and by different tension of their fibrous rings.

A *systolic murmur*, probably due to relative mitral insufficiency, is frequent. The formation of eddies in an overloaded and distended ventricle could also be considered as a possible cause.

The 2d sound shows changes in time and amplitude, and it may be split. The sound is delayed in regard to the 1st sound because of prolongation of mechanical systole, but may precede the end of the T wave on account of even more prolonged electrical systole. An occasional increase of the 2d sound occurs when the P wave coincides with the end of the T wave. *False splitting* occurs if an atrial sound falls just before the 2d sound, *true splitting* when two valvular components are separate. The former shows the low-grade vibrations of the atrial sound, the second has two groups of similar vibrations.

Triple rhythms have the usual graphic characteristics. The additional sound occurs periodically. It may occur intermittently every time that a P wave follows the T wave, i.e., any time that the atrial contraction coincides with rapid ventricular filling.

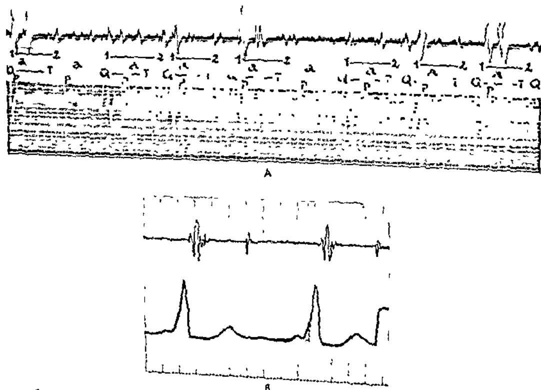


Fig 11-22. A. Incomplete AV block with Wenckebach periods. Phonocardiogram (stethoscopic) 516. B Wolff-Parkinson-White syndrome Phonocardiogram 0–25 cps 517.

Graphic tracings in arrhythmias and atrioventricular block

ALDO A. LUISADA

SUPRAVENTRICULAR TACHYCARDIA

Jugular Tracing. There is only one high wave, owing to fusion of the various waves If the atrial and ventricular contractions occur exactly at the same time, this venous wave becomes high, because if the right atrium cannot push the blood forward against the closed tricuspid valve, it will push it backwards, into the large veins

Arterial Pulse. The pulse becomes small during the attack. The dicrotic wave, however, may be relatively higher, and its fusion with the following pulse wave may simulate an anacrotic pulse The speed of the pulse wave is often reduced

VENTRICULAR TACHYCARDIA

Jugular Tracing. High atrial waves are recorded, at a rate which is slower than that of the arterial pulse (unless there is atrial fibrillation). The waves may be slightly irregular

Arterial Tracings. The pulse waves are small and may show a variable height, then, a higher wave is caused by the casual precedence of an atrial contraction over a ventricular. There may be *pulsus alternans.*

ATRIAL FLUTTER

Low-frequency Tracing of the Precordium. Atrial waves may be recorded in the intervals between the ventricular waves of this tracing.

Jugular Tracing. Regular atrial waves were recorded by several workers. More recently, Contro has recorded high atrial waves in five cases of flutter by means of a linear microphone and an amplifier. These waves give evidence of the coordinated contractions of the atria.

Electrokymogram. If the slit of the pickup is placed across the border of either atrium, good evidence of atrial contractions can be secured (Fig. 11-18A, B). The atrial waves are usually of large amplitude, and their detection is important in cases where the electrocardiographic tracing had led to admission of "impure fibrillation."

ATRIAL FIBRILLATION

Jugular Tracing. The C and V waves follow each other with complete irregularity. There are no A waves, because of the fibrillation

Low-frequency Tracing of the Precordium. The waves caused by ventricular contraction are of various height and configuration. When diastole is short, the subsequent isometric tension period becomes longer. The height of the waves varies somewhat but is not exactly proportional to the length of the preceding diastole.

Arterial Tracings, Hemodynamics. The pulse waves are typically irregular, having various heights, lengths, and configurations Patients in congestive failure often have a *pulse deficit* because some of the ventricular contractions have such a small ejection that they are not followed by a pulse wave. However, when ejection is small, waves may be present in the

Atrioventricular Block with Mitral Lesions. The valvular lesion frequently causes the 1st sound to be less decreased than when the mitral valve is normal. The systolic murmur of mitral insufficiency may decrease or disappear if there is a short P-R interval; this is because atrial contraction somewhat resists the regurgitant jet (only for a short time) and gives a greater tension to the mitral ring. Every atrial contraction may be followed by a *murmur,* during the long diastole, three or four murmurs may be seen with regular intervals and progressively decreasing amplitude. This is because the increased diastolic filling of the ventricles gradually hinders further filling due to atrial propulsion.

Incomplete Atrioventricular Blocks. In a 2:1 block, one may see *two atrial sounds,* one in protodiastole and one in presystole (Fig. 11-21C) The former may coincide with and accentuate the 2d sound, it may fall during rapid filling, thus causing a summation type of triple rhythm, or it may give a delayed diastolic sound. In cases without valvular lesions, every P wave may be followed by an atrial murmur, as in complete AV block, in cases with mitral stenosis, the P wave may be followed by a loud diastolic murmur. In both cases, a short systolic murmur is also usually present. In *Wenckebach periods,* the diastolic atrial sounds parallel the cyclic variations of the P-R interval. This holds true both for the presystolic murmur of mitral stenosis and for the atrial sounds and murmurs in cases without valvular lesions (Fig 11-22A). The magnitude of the 1st sound varies according to the duration of the P-R interval; it may become progressively decreased, accentuated, or split.

FIRST DEGREE OF ATRIOVENTRICULAR BLOCK Phonocardiographic evidence of atrial activity (sounds, murmurs) occurs earlier in regard to the 1st sound. If tachycardia is present, such murmurs may even become mid- or early diastolic. Thus, they may coincide with the opening snap of the mitral valve, with a 3d sound, or with the early diastolic murmur of mitral stenosis Unusual auscultatory rhythms may arise in this way.

Wolff-Parkinson-White Syndrome. Only a few phonocardiograms have been published to date. The interval Q-1st sound is normal; the 1st sound has a normal magnitude (Fig 11-22B). The 2d sound is neither split nor delayed. A 3d sound may be recorded. These data may be interpreted as indicating that (1) there is no bundle branch block (in the normal sense), (2) the P-R interval is only apparently shortened, (3) AV valves closure occurs at a normal distance from the P wave, in spite of the so-called *delta wave.*

8

Phonocardiography in arrhythmias and blocks

ALDO CALO

SUPRAVENTRICULAR TACHYCARDIA

The findings during the attack should be considered separately from those obtained after reestablishment of *sinus rhythm*. The latter may be considered as the result of a posttachycardial phonocardiographic syndrome

The Attack. Increased loudness of the 1st sound is frequent Even though loudness may progressively increase during the first few beats of the attack, once the maximum loudness has been reached, the 1st sounds continue with the same magnitude, small variations in amplitude may be due to respiratory variations The increased loudness of the 1st sound may be caused either by summation of the 1st *with the 4th (atrial) sound, or by changes in the mechanism of closure of the AV valves*

In *low nodal tachycardia with retrograde conduction*, the atrial sound may show up in the tracing soon after the 1st sound, causing *splitting of the 1st sound* (Fig. 11-19A). Actually, it is not a real splitting but the addition of a new sound (atrial) in early systole *Alternans is exceptional* If present in the above cases, alternans affects only the ventricular component, i e, the 1st sound, while the atrial sound is unaffected. The *2d sound* may be accentuated, split (either occasionally or *continuously*), or small, to the point of disappearance. Both *systole and diastole* are markedly shortened, the latter more than the former As diastole becomes progressively shorter and the atrial contraction is closer to the rapid filling of the preceding cycle, a *summation type* of triple rhythm (summation gallop) occurs. Several *murmurs* may appear during attacks of tachycardia of long duration. They have been explained as the result of increased speed of flow, changes of the normal sequence of atrial and ventricular contractions, or relative insufficiency of the mitral valve The latter might be due to ventricular dilatation as a result of strain On the contrary, preexisting murmurs caused by valvular lesions or shunts may disappear during an attack

Posttachycardial Syndrome. The phonocardiographic signs of this *syndrome may consist of changes of the sound and murmurs present* before the attack; disappearance of signs brought about by the attack itself; return of signs obscured by the attack, and, finally, appearance of new phonocardiographic data. *After sinus rhythm is reestablished, the following may be found: 1st and 2d sounds—true or* false splitting, alternans may either decrease or disappear. Systole and diastole regain their normal values A *summation type of triple* rhythm, originated by the attack, may disappear. On the other hand, a new triple rhythm *may appear after the attack because of myocardial insufficiency.* The same may be said for murmurs which may disappear, reappear, or start after the attack *These murmurs are* usually of mitral origin and are functional

ATRIAL FLUTTER

In *most cases, the atrial sounds,* which on occasion may become abnormally large and even *clinically audible, may have no time re-*

Bundle branch and intraventricular block

Bundle Branch Block; Intraventricular Block
AARON B. BENCHIMOL AND PAUL SCHLESINGER

Graphic Data in Bundle Branch Block
ALDO A. LUISADA

BUNDLE BRANCH BLOCK

MODERN CONCEPTS OF VENTRICULAR ACTIVATION

The bundle branch block concept rests upon the knowledge of the process of ventricular activation which takes place in the conducting tissues of the heart, originating in the SA node, spreading through the atria to the AV node, the bundle of His and its two stems, and finally reaching the myocardial fibers through the subendocardial Purkinje network

When one of the branches of the bundle of His fails to conduct the stimulus, the order of ventricular activation is modified and certain electrocardiographic changes appear which are characteristic of the various types of bundle branch block These abnormalities depend not only upon whether the right or the left bundle branch is involved but also upon the severity of the lesion and the degree of conduction disturbance.

According to studies of Sodi Pallares et al (1956), the first part of the ventricular myocardium to be activated is the interventricular septum, which is no longer considered as a syncytial mass, but rather as *two separate portions, separated by a barrier," in which the muscle fibers are diversely oriented with multiple synaptic connections,* in addition, these septal fibers have different polarities

The greater part of the septum belongs to the left ventricular myocardium, so that it forms the entire posterobasal aspect of the septum, which is completely devoid of right ventricular fibers. Thus, the left ventricle encroaches upon certain areas of the endocardial surface of the right ventricle, and an electrode placed at this point may actually record left ventricular potentials. The right ventricular component of the septum represents only a minor fraction of its entire mass.

The interventricular septum is activated from both the right and left endocardial surfaces *The left bundle branch is responsible for the activation of the entire left septal surface, as well as for most of the septum proper, whereas the right branch supplies a very small portion of this structure*

Since the left ventricular septal mass is greater than that pertaining to the right ventricle, it is obvious that the resultant vector is directed from left to right

The beginning of ventricular activation takes place at the middle third of the septal surface, and spreads from left to right, anteriorly and upwards The last points to be activated are the anterobasal portions of the right septal surface

The right surface of the septum is normally activated 0 01 sec after the left, whereas the last portions are activated 0 03 sec later (Fig. 11-23A).

The initial septal vector is responsible for the small Q wave which is usually recorded in the leads overlying the left ventricle, and which is due to activation of the left septal mass This process

(earlier contraction of the right ventricle, subsequent contraction of the left, responsible for the pulse).

The *stroke volume* varies greatly, being inversely proportional to the length of the preceding diastole. Therefore, the earlier the contraction, the smaller the stroke volume. The compensatory pause is followed by a contraction which has a proportionally larger stroke volume. This, however, is not true if the myocardium is weak.

The speed of the pulse wave is directly proportional to the level of diastolic pressure; therefore, the weak pulse of the premature contraction has a greater velocity than the others.

Blood Pressure Tracings. Different levels of blood pressure can be obtained if the premature beats occur periodically. (1) those corresponding to the systolic and diastolic pressure of the normal pulse waves, (2) those corresponding to the pulse waves of the premature beats (low systolic, high diastolic); and (3) those corresponding to the pulse waves immediately subsequent to the premature beats (high systolic, low diastolic).

Low-frequency Tracing of the Precordium. The premature contraction may give waves of normal configuration The isometric tension period is often prolonged. This may cause bizarre or large waves.

Electrokymogram. Premature contractions are easily studied by means of border tracings of the left ventricle, the pulmonary artery, or the aortic arch If simultaneous tracings of the left ventricle and one of the arteries (aorta or pulmonary artery) are taken, conclusions may be drawn about the site of origin of a ventricular premature beat. The aspect of the tracing depends upon the time of the cardiac cycle at which the premature contraction occurs and the phase of the ventricular filling

If the contraction starts early in diastole, its amplitude is small, isometric contraction is prolonged, and the curve assumes a more peaked aspect. The isometric tension period may last more than 0.06 sec on account of both the high level of arterial pressure and the small amount of ventricular blood If the contraction takes place immediately after the T wave, no ejection may occur During the compensatory pause, an abnormally large filling of the ventricles takes place. This, plus the lower level of arterial pressure, causes a shortening of the isometric tension period of the following contraction.

ATRIOVENTRICULAR BLOCK

Jugular Tracing. The A waves are normal in shape and follow each other, usually, at a normal rate; the C and V waves occur at regular, but much longer, intervals. Therefore, more than one A wave is found between a V wave and the next C wave. Occasional coincidence of an A wave with a C or V wave may occur, with a resulting higher wave.

Arterial Tracing. A high and slow pulse is recorded. An anacrotic depression is frequently present in the ascending branch of the pulse curve. Multiple undulations follow the dicrotic wave.

In *occasional block*, the tracings reveal the occasional absence of a pulse wave (*intermittence*). In *periodic block*, the series of pulse waves shows a periodic increase in the pause separating two pulses, then a longer pause with a deeper pressure drop. *Interference dissociation* may cause a bigeminal rhythm, the second wave being paradoxically *higher* than the first (Fischer).

Low-frequency Tracing of the Precordium. High atrial waves are present between the waves caused by the ventricular contractions

Electrokymography. The electrokymogram of AV block has been studied by the author, Engstroem et al., and Pannier et al

ATRIAL TRACINGS If atrial contraction falls during ventricular systole, the atria decrease in volume as in normal subjects; apparently the blood is pushed backwards into the veins. If the atrial contraction falls during ventricular diastole, the pattern consists of an oblique, descending line during atrial contraction, and a less steep rise subsequent to it. The depth of the contraction varies, it is usually larger when the atrial contraction falls during a ventricular contraction because of additional ventricular pull (Fig. 11-18C).

LEFT VENTRICULAR TRACING. The tracing of the left ventricle may not show any effect of the atrial contractions. If it does, the latter are revealed by small positive waves.

is initiated at the left ventricular endocardium and spreads toward the septal fibers at the base of the anterior papillary muscle of the right side of the septum, which at this level is probably still formed by the left ventricle.

The late activation of the basal portions of the septum is due to the scarcity of the Purkinje network at this level. It probably contributes to a great extent to the third cardiac vector (so-called "final vector"), although this is variable from one individual to the other.

Following the initial septal activation, the depolarization process spreads to the free walls of both ventricles perpendicularly, from the endocardium to the epicardium. Studies of Prinzmetal et al (1953) confirmed by Sodi Pallares (1956) have demonstrated that approximately two-thirds of the subendocardial aspects of the free walls of both ventricles are simultaneously and almost instantaneously activated, having practically no electrocardiographic representation The potentials obtained in this area are similar to those recorded in the ventricular cavities, this portion of the myocardium was designated as the *electrical endocardium,* since from the standpoint of cardiac activation, it merely represents an extension of the cavity The spread of excitation through the electrical endocardium is extremely rapid, having an approximate speed of 2,000 to 4,000 mm/sec This is explained by the deep penetration of the Purkinje fibers into this part of the cardiac muscle.

The activation of the free wall of the ventricles is responsible for the second cardiac vector, which is primarily due to the predominance of electrical forces of the left ventricle, ten times greater than those of the right ventricle, the latter being insignificant from the standpoint of the vectorial analysis of the electrocardiogram in normal individuals (Fig. 11-23B).

This second cardiac vector is generally of great magnitude, is directed toward the left, posteriorly and downwards, and is seldom influenced by the right ventricle (this may occur in cases of extreme right ventricular hypertrophy). The predominance of the electrical forces of the left ventricle in cardiac activation explains the counterclockwise rotation of the normal vectorcardiogram in the horizontal plane.

The process of activation varies according to the degree of block. Thus, it becomes important to distinguish between *complete and incomplete bundle branch blocks.* This concept was established on the basis of experimental studies (Rodriguez and Sodi Pallares), by comparing the electrocardiograms obtained in dogs with various degrees of bundle branch block, and those of a human being's tracing with

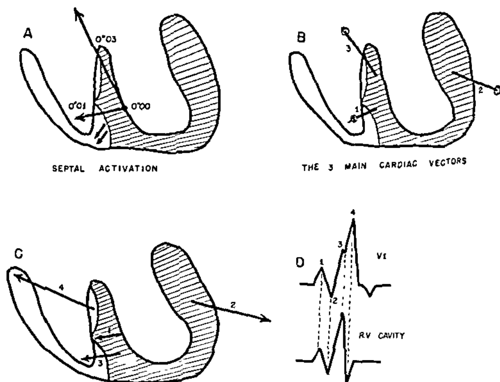


Fig. 11-23. A Septal activation. B The three main cardiac vectors C and D. Schematic representation of the four vectors resulting from ventricular activation in right bundle branch block, and the corresponding deflections in lead V_1 and in the right ventricular cavity.

lationship with the main heart sounds. In other cases, changes of cardiac sounds, murmurs, and intervals may be produced by a profound alteration in the hemodynamics caused by the disturbance of rhythm (Fig. 11-19B). The atrial sounds recorded from the esophagus start 0.04 sec after the P waves, most likely they are produced within the atria. The atrial sounds recorded over the precordium are far more delayed because they start from 0.14 to 0.24 sec after the P waves and 0.10 sec after the A waves of the jugular tracing. This indicates that the precordial atrial sounds are originating either in the ventricular walls or in the AV valves. In general, each atrial sound consists of a single group of 1 to 4 low-pitched vibrations, *lasting from 0.03 to 0.08 sec.* Exceptionally they last 0.16 sec and present two separate components, one with a single high vibration, and the other with several lower vibrations (see Atrioventricular Block, further on in this chapter, for explanation). The amplitude of atrial vibrations is usually small, but in certain cases they may be one-half of either heart sound. Sounds produced during systole are often higher than those originated in diastole. In irregular flutter, the amplitude of these sounds is variable and some of them may be absent in spite of ECG evidence of atrial contractions. The modifications of cardiac sounds, murmurs, and intervals produced by *regular flutter* are constant, while variable and inconstant findings are found in *irregular flutter*, where marked changes of dynamics occur.

The changes of the 1st sound are closely related to the duration of the P-R interval or P-1st sound interval, which are equivalent. For values between 0.08 and 0.12 sec, the 1st sound is increased in loudness (an occasional increase is typical of irregular flutter). For higher or lower values, the 1st sound either may be decreased or may present a systolic or presystolic addition of an atrial sound (*pseudo splitting*). The *1st sound* may be delayed over the beginning of the QRS complex, may be of small amplitude, and may be alternating. The *2d sound* may be increased, decreased, or split. In irregular flutter an occasional accentuation may be due to addition of an *atrial sound* to the 2d sound. At times, the 2d sound may disappear because of weak ventricular systole, as in some types of extrasystoles or cases of atrial fibrillation. A summation type of triple rhythm can take place whenever an atrial contraction coincides with the phase of rapid ventricular filling. In regular flutter, this may happen after every ventricular systole; in irregular flutter, it may happen occasionally.

It is a common notion that the *presystolic murmur* of mitral stenosis disappears whenever the left atrial contraction fails to occur. The fluttering left atrium may display such a powerful systole as to accelerate the flow across the mitral valve. This results in *a loud murmur for every atrial contraction* which takes place in diastole (in systole, it is obvious that the atrium cannot open the mitral valve). The *systolic murmur* of mitral insufficiency may *disappear or change* in character during atrial flutter, and it may reappear or increase after reestablishment of the sinus rhythm.

ATRIAL FIBRILLATION

Atrial fibrillation is characterized by a complete arrhythmia of cardiac sounds and murmurs with irregular variations for every cycle. An exception is represented by rare cases with idioventricular rhythm.

Cases without Valvular Lesions. The 1st sound is usually *delayed* over the R wave but this delay is *small.* Its amplitude and duration are variable, so that the 1st sound may become quite small or very large. Apparent splitting is frequent; this may be due to a separation of the valvular components or, in the case of a very short diastole, to the occurrence of a ventricular type of triple rhythm (gallop) immediately followed by the 1st sound (Fig. 11-19C). The 2d sound usually presents continuous changes of amplitude and duration which are independent from those of the 1st sound. There also may be an occasional splitting due to asynchronism of the semilunar valves.

In some cases, the apical phonocardiogram may show *a short systolic murmur,* which, in the absence of any valvular lesion, is thought to be due to functional mitral insufficiency or to the formation of eddies. Even though no atrial or summation type of triple rhythm may occur on account of the lack of atrial contractions, various types of triple rhythm may occur. These are due to the addition of a ventricular sound which may fall in early diastole, mid-diastole, or just prior to the following 1st

similar configurations. It was observed that the *complete section* of one of the branches of the bundle of His was followed by a remarkable increase in the *duration* of the QRS interval and by a considerable delay in the intrinsicoid deflection, with secondary T-wave changes over the homolateral ventricle, in addition to a prolongation of electrical systole. These changes were characteristic of the complete type of bundle branch block. If instead of making a complete section, *the upper part of the interventricular septum (where the bundle branch crosses this area)* was compressed, it was observed that for short periods of time, QRS complexes were recorded similar to those of the previous experiment, the latter became progressively normal, with an intermediate stage during which a configuration similar to that of complete bundle branch block was obtained, although of shorter duration, these were designated as *incomplete bundle branch blocks.*

Notwithstanding the number of objections to the concept of bundle branch block in man, especially that of its septal mechanism, the above configurations represent, in the majority of cases, various degrees of conduction disturbance in one of the branches of the bundle of His causing ventricular asynchronism. This concept has been confirmed experimentally, pathologically, by intracavitary tracings and precordial leads, and by mechanical recordings showing ventricular asynchronism. Studies of Sodi Pallares on the mechanism of septal activation and experimental bundle branch block have contributed a great deal to a better understanding of this problem, confirming and extending knowledge of these conduction disturbances.

VENTRICULAR ACTIVATION IN BUNDLE BRANCH BLOCK

Right Bundle Branch Block. In all degrees of right bundle branch block, including the complete type, the wave of excitation crosses the left septal mass, which forms the majority of the septum, following the normal pathway with no change either in direction or velocity (1,000 to 1,200 mm/sec). However, there is a *late arrival* of the wave of excitation to the right side of the septum, with a considerable delay (0.06 *sec instead* of 0.01 to 0.02 sec) after the activation of the left side. This conduction delay is due not to uniform slowing of the wave of excitation *in* the entire septal mass, but rather to slower progression in a small area of the myocardium which is very close to the right surface, forming a "barrier" which separates the regions normally supplied by the left bundle branch from the area activated by the right branch. This has been proved experimentally by Sodi Pallares et al (1956) using bipolar leads, with the electrodes placed very close to one another, and including the intramural potentials.

From a vectorial point of view, four main vectors can be schematically identified in right bundle branch block representing the sequence of ventricular activation in these cases (Fig. 11-23C, D).

Vector 1 corresponds to the *normal septal vector,* since this phase of the activation process is unaltered in right bundle branch block, and determines the small Q waves in leads overlying the left ventricle, as well as the small initial positive deflection obtained both in the cavity of the right ventricle and over its epicardial surface.

Vector 2 represents the *activation of the free wall of the left ventricle* and is responsible for a small S wave recorded in the *right ventricular* cavity and over the right ventricular *epicardium,* since it is directed from right to left.

Vector 3 corresponds to the *powerful septal forces which are directed from left to right in the lower part of the septum,* and which develop when the wave of excitation crosses the barrier between left and right septal masses with a considerable delay. This vector is of great magnitude, as it is due to a slow type of activation, and it is well known that the slower the velocity of the excitation wave, the more powerful are the corresponding vectorial forces. In view of its great magnitude, it partially neutralizes the previous one corresponding to the activation of the free wall of the left ventricle, and explains the small amplitude of these forces. The third vector is responsible for the right intracavitary R′ and for most of the initial segment of the right epicardial R′.

Finally, *vector 4 probably represents a summation of the activation of the upper portions of the septum and the free wall of the right ventricle,* determining the peak of R′ over the right ventricular epicardium and that of *S′* recorded in the cavity of the right ventricle.

Left Bundle Branch Block. In right bundle branch block, *it is* difficult [illegible] *from left to right,* as in normal individuals. Thus, it is *impossible* to detect the exact instant when the *activation* crosses the

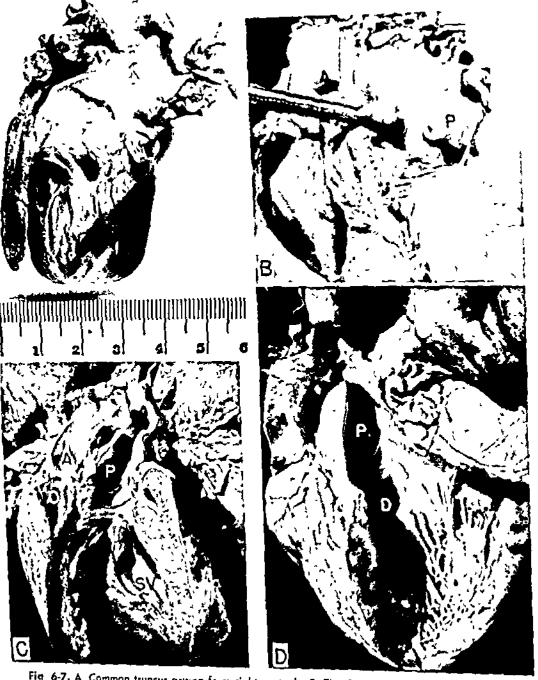


Fig 6-7. A Common truncus arising from right ventricle. B. The *Taussig Bing heart. Right ventricular view A, aorta, P, pulmonary artery* C. Complete transposition with single ventricle and small outlet chamber. *SV*, single ventricle, *O*, small outlet chamber; *A, aorta; P, pulmonary artery.* D Complete transposition with normal architecture. Left ventricular view. *P*, pulmonary artery; *A*, aorta, *D*, defect of ventricular septum (A. B. *From M. Lev. Autopsy Diagnosis of Congenitally Malformed Hearts. Charles C Thomas,* 1953.)

ing a pseudoseptum between the aorta and pulmonary artery

PATHOGENESIS OF THE COMPLEX. The basic anomaly may be considered to be the abnormal position of arterial trunks, together with an *absence of the ventricular septum* Hence, if there is no impediment to flow of blood, the pulmonary artery would be large and the aorta small However, there is often an associated *hypoplasia of the pulmonary tree,* hence a de-

fills in the gap between the aorta and the anterior leaflet of the tricuspid.

PATHOGENESIS OF THE COMPLEX. We may again look upon the position of the aorta as the primary defect, with the narrowing of the pulmonary tract and the ventricular septal defect as secondary (see Chap 1). The right ventricle presents a pressure hypertrophy, since it is contracting against the combined (Lev, 1953) systemic resistance and the resistance of the pulmonary stenosis. The size of the left atrium and left ventricle is related to decreased flow.

Partial Transposition with Aortic Hypoplasia (Eisenmenger Type). This anomaly (Lev, 1953) resembles the Eisenmenger complex except that the aorta emerges only from the right ventricle, instead of in a straddling position (Fig 6-6C, D) The right ventricle is more hypertrophied than in the Eisenmenger complex.

PATHOGENESIS OF THE COMPLEX The basic anomaly again is the position of the vessels and the limited aortic tree. The right ventricle is more hypertrophied than in the Eisenmenger complex because there is more flow into the right ventricle. Even though the aorta emerges completely from the right ventricle, it does not necessarily receive blood from this chamber.

Common Truncus from the Right Ventricle. Here the right ventricle is more hypertrophied and the left ventricle smaller than in the overriding truncus (Lev and Saphir, 1945)

Overriding Pulmonary Artery (the Taussig-Bing Heart). In this complex (Taussig and Bing, Lev and Volk), the large pulmonary artery straddles the ventricular septum over a defect, thus emanating to a varying extent from both ventricles (Fig 6-7B) The small aorta emerges from the right ventricle away from the defect. The right ventricle is hypertrophied, while the left atrium and ventricle are increased in size, and hypertrophied or normal in thickness. The septal band is connected by a small ridge to the parietal band, which represents a thick bifurcated structure. One part of the parietal band passes from the septum to the anterior wall. The other part lies beneath the aorta. The coronary distribution is typical of partial transposition Pulmonary arterial and arteriolar changes are common.

PATHOGENESIS OF THE COMPLEX The basic anomaly may again be considered to be the abnormal position of vessels (see Chap 1) and their relationship to the defect. The right ventricle presents a combined pressure and volume hypertrophy due to the effects of the ventricular septal defect and the left-to-right shunt at this level. The left atrium is enlarged because of increased flow. The left ventricle may be normal or increased in size and thickness, depending upon the opposite factors of increased flow and diminished peripheral resistance. In a variant of this anomaly, there is a functional pulmonary stenosis with normal pulmonary flow.

Complete Transposition with Normal Architecture. In this complex (Lev, 1953; Taussig, 1938), the aorta and pulmonary artery emerge from the wrong ventricles (Fig. 6-7C). There is an associated patent foramen ovale, and there may be a ventricular septal defect or patent ductus arteriosus, instead of or in addition to the foramen ovale. The right ventricle is hypertrophied, while the left ventricle may be enlarged or normal in size. The aorta and pulmonary artery may be normal in size, but either may be larger or smaller than normal The muscle bundles of the right ventricle may be normal in architecture, or the septal or parietal bands of the crista may be hypertrophied The left and right coronary ostia lie in the right and left posterior sinuses of Valsalva, thus being rotated counterclockwise, looking ventricle-ward from the aorta. The coronary arteries in general take over the distribution of the opposite artery. The right auricular appendage may be displaced behind the arterial trunks

PATHOGENESIS OF THE COMPLEX. The primary anomaly may be considered to be the abnormal position of the arteries The right ventricle presents a pressure hypertrophy, being related to systemic resistance There is usually increased pulmonary flow, hence the left side of the heart may be enlarged

Complete Transposition with Cor Biatriatum Triloculare. In this complex, both the aorta and the pulmonary artery emerge from a *common ventricle*, into which enter the mitral and tricuspid valves The arterial trunks are in a transposed position, and either may be hypoplastic or atretic Usually, it is the pulmonary artery which is small There is usually a small remnant of the ventricular septum The crista supraventricularis may be hypertrophied, form-

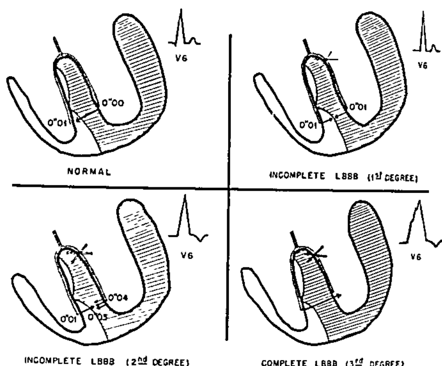


Fig. 11-24. Septal activation in the normal heart and in the three degrees of left bundle branch block with the corresponding ventricular complexes in the left precordial leads.

septal barrier However, this does not apply to left bundle branch blocks, in which different types of activation are observed in relation to the degree of this conduction defect. According to Rodriguez and Sodi Pallares, three types of left bundle branch block must be distinguished (Fig. 11-24):

1. *First degree* There is only a slight delay in the spread of the stimulus in the left branch of the bundle, resulting in a *late activation of the left septal surface*, without any change in the direction or speed of the excitation wave throughout the septal mass Since under normal circumstances, the activation of the left septal surface precedes that of the right by 0.01 to 0 02 sec, when a slight delay in the transmission of this wave occurs in the left branch (approximately 0 01 to 0 02 sec) both sides of the septum are simultaneously activated and consequently no Q wave is recorded.

2 *Second degree* In these cases, there is a greater delay of the conduction of the stimulus in the left branch, which nevertheless continues to transmit the impulse at a much lower speed Thus, the beginning of the left septal activation is recorded with a delay of 0.04 sec and is preceded by the right septal forces. *Septal activation occurs, therefore, in an opposite direction to normal, although only partially so.* The activation of the interventricular septum begins over the right septal surface and proceeds *from right to left;* if the barrier is transposed, the two septal forces will meet one another 0.04 sec later. It can be seen, therefore, that most of the septal activation proceeds from right to left, although this does not occur throughout the entire activation process, at the end of this process, late septal forces play a role and are directed from left to right. In this type of block, the Q wave, representing the normal first septal vector, disappears; there also is a slurring of the upstroke of R over the left ventricular epicardium. This represents the initial inverted activation of the septum (from right to left) and coincides with the initial r wave in the left ventricular cavity

3 *Third degree (complete left bundle branch block)*. In this type, the left branch is completely interrupted and is functionally incapable of transmitting the excitation wave. *The right branch activates the entire septal mass in an opposite direction to normal, i.e., from right to left.* Septal depolarization is a comparatively slow process and takes place at an average speed of 300 mm/sec, which is similar to that of the spread of activation in the myocardial fibers themselves. This alone, however, does not explain the great delay of activation on the left side of the septum as compared

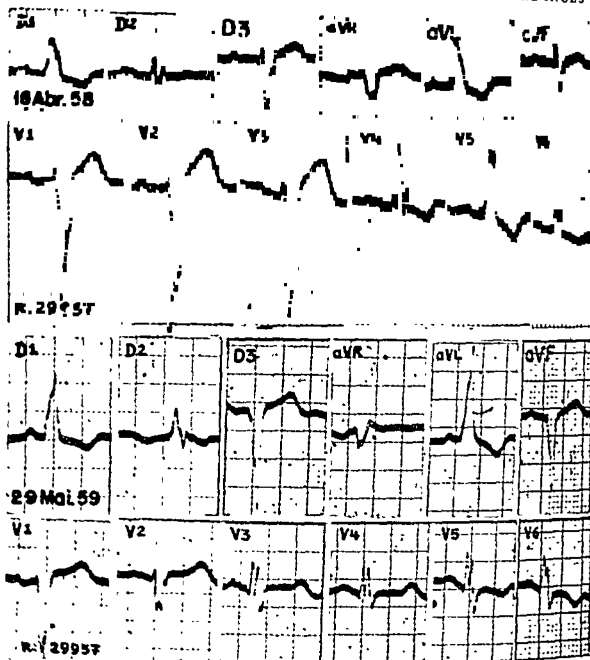


Fig. 11-30. Electrocardiogram of a 60-year-old patient with arteriosclerotic heart disease, showing complete left bundle branch block in the upper tracing. Bilateral internal thoracic artery ligation was performed for the relief of angina pectoris in June, 1958. In May, 1959, the patient sustained an acute coronary thrombosis; the ECG recorded 4 weeks later (lower tracing), shows deep S waves not previously present in leads V_5 and V_6, probably because of the transmission of the left intracavity potential (RS) to the exploring electrode through the area of necrosis.

have been reported in the course of *digitalis intoxication* (Benchimol, 1944) It is possible that these cases may be due to a vagal influence, although it is believed by most authors that a direct toxic effect on the conduction tissue, such as occurs in cases of *myocarditis*, is probably responsible.

In clinical practice, when an intermittent type of bundle branch block is recorded, it often appears or disappears following physical effort, amyl nitrite inhalation, or atropine injection.

Vagal stimulation obtained by ocular compression may cause the block to disappear, as in Fig 11-31. This is not a direct vagal effect upon the bundle branch, but rather an indirect [illegible]

[illegible] of the bundle branch system.

These types of intermittent bundle branch

with the right (approximately 0.07 to 0.08 sec)

According to Sodi Pallares (1956), the inverted activation of the interventricular septum is retarded at ... ...ally, there is a delay at the ba... w... is ... in ...

opposite direction to that normally ... finally, the third delay occurs upon arrival of the activation wave at the left septal surface, which acts as a second barrier. These points of delay explain both the widening of the QRS complexes and the slurring and notching of its various components which are characteristic of the complete left bundle branch block. In all degrees of left bundle branch block, notwithstanding the marked alterations in septal activation (which is not only delayed but often completely inverted in direction), the activation of the free wall of the left ventricle remains unchanged, although it begins later than normal, because of the delay that occurs in the interventricular septum.

It has not been possible to confirm the abovementioned concept of these partial types of left ventricular conduction defect by the vectorcardiographic analysis of the incomplete types of left bundle branch block. In cases with electrocardiographic signs suggestive of incomplete left bundle branch block, the horizontal plane VCG has shown a counterclockwise rotation.

THE ELECTROCARDIOGRAM IN BUNDLE BRANCH BLOCK

The general characteristics of the bundle branch blocks consist of widening of the QRS complexes with slurring and notching of its various waves, delay of the intrinsicoid deflection in leads corresponding to the homolateral ventricle, prolongation of electrical systole, and secondary T-wave changes. It is to be emphasized that in addition to the characteristic contours of the electrocardiogram, the practical diagnosis of right or left bundle branch block requires certain data for a more precise recognition of those conduction defects, such as a supraventricular pacemaker, a P-R interval above 0.12 sec, and a typical configuration in the precordial leads. Thus, the diagnosis of bundle branch block cannot be made in the presence of complete AV block; on the other hand, a P-R interval below 0.12 sec with a widened QRS complex usually corresponds to the Wolff-Parkinson-White syndrome. A complete set of precordial leads usually permits a precise identification of the bundle branch involvement, which is often difficult on the basis of the standard leads alone, especially in cases of left bundle branch block in vertical hearts, or right bundle branch blocks in horizontal hearts.

All types of bundle branch block may be *permanent* or *intermittent*; in the latter group are included cases in which the conduction defect is *transient*, with normal and aberrant QRS complexes recorded in the same tracing.

In some instances, the electrocardiogram may show alternating complete and incomplete bundle branch block, a fact in favor of the general concept of the incomplete types of conduction defect.

Complete Right Bundle Branch Block. In right bundle branch block, the initial septal vectors are directed from left to right (as in the normal heart) and the main abnormality occurs in the final vectors. The study of the unipolar, epicardial, and intracavitary potentials in right bundle branch block has led to a better understanding of the changes observed in standard and precordial leads.

Intracavitary leads in right bundle branch blocks were recorded by Sodi Pallares et al. (1948b), in dogs as well as in human beings, and the configurations obtained corresponded to those calculated by the vectors of cardiac activation. Thus, in the right ventricular cavity, rsR'S' complexes were recorded, whereas in the left ventricle, the tracing was essentially a QS wave with notching and slurring of the descending limb (Fig. 11-25).

An important point to remember is that a part of the free wall of the right ventricle corresponding to the trabecular zone is very thin and rarely exceeds 2 mm; leads V_2 and V_3, which usually overlie this area, record potentials closely resembling those of the right ventricular cavity. This configuration is generally rsR'S', which is explained by the direction and magnitude of the main vectors ... ...ndle branch ... reference to ... ...ortion of the free wall of the right ventricle corresponding to leads V_1 and V_2, the configuration is rsR', with a notching of the upstroke of the R' wave. This shows the great delay in the intrinsicoid deflection over the right ventricular activation which occurs in right bundle branch block.

The r and s waves correspond to vectors 1 and 2 and coincide with the two initial intracavitary deflections. The initial portion of R' is due to the

blocks, clinically observed, may appear gradually, resembling those obtained experimentally; a number of transitional complexes of incomplete bundle branch block are recorded preceding the final appearance of the complete . . . These tracings, oc-

dle branch block as previously described. . . casionally, normal conduction alternates with bundle branch block, either regularly (2:1; 3:1; 3:2, etc.) or irregularly, without any apparent cause Such tracings are usually designated as *intermittent bundle branch block* and offer a unique opportunity for the study of the secondary changes in ventricular repolarization

BUNDLE BRANCH BLOCK AND MYOCARDIAL INFARCTION

The association of bundle branch block with myocardial infarction is not rare, although certain types of block may obscure the electrocardiographic recognition of infarction. The problem differs according to the type of block.

In *right bundle branch block*, the evidence of an associated infarction is not difficult to determine This has been shown experimentally in dogs by cutting the right bundle branch and ligating the anterior descending branch of the left coronary artery The tracings obtained in human beings are essentially similar to those of

ciated with Q or QS waves due to transmission of the initial negativity of the left ventricular cavity to the epicardial surface over the region of the infarct This is because in right bundle branch block, there is no change in the initial vectors of ventricular activation Thus, the left ventricular cavity maintains its negativity, which, in cases of localized necrosis of the anterior or posterior wall, is transmitted to the epicardial surface *In anterior infarcts*, the diagnosis is based upon abnormal Q waves in precordial leads. In *anteroseptal lesions*, these deflections are seen in leads V_1 to V_4 and the rsR' configuration is changed to QR with an increased duration of the Q wave (Fig. 11-33C) *In anterolateral infarctions*, the abnormal Q waves are recorded in the left precordial leads, and often in leads I and aVL (Fig. 11-29). Finally, *in posterior infarctions*, the diagnosis is based upon abnormal Q waves in leads II, III, and aVF, in addition to the characteristic right bundle branch block pattern in precordial leads. As for the evidence of *injury* and *ischemia*, they are important diagnostically only during . . . stage of infarction and, in the cour . . .

since . . . may show S-T-segment changes and T-wave abnormalities in the absence of infarction.

according to the site of necrosis (in the . . . in the free walls of the ventricles). These studies have shown that abnormal Q waves in leads V_1 and V_2 denote *an infarct of the middle third of the septum*, whereas similar deflections in V_3 and V_4 indicate low septal infarctions. Deep Q waves in leads V_5 and V_6 are characteristic signs of involvement of *the free wall of the left ventricle*. When the infarct is located in the free wall of the right ventricle or in the upper part of the septum, there are no definite electrocardiographic signs that can be considered diagnostically significant. Some types of infarction included in this classification correspond to a combination of those previously described

It should be emphasized that cases of right bundle branch block with right atrial dilatation often exhibit in leads V_1 and V_2 a qR configuration with a delayed intrinsicoid deflection, which may lead to the erroneous diagnosis of right bundle branch block complicated by anteroseptal infarction The differential diagnosis is established by the clinical data, by the progressive ST-T changes, and possibly by the presence or absence of Q waves in left precordial leads, since in cases of midseptal infarction the disappearance of the initial septal vector results in the absence of Q waves in left precordial leads

In the presence of *left bundle branch block*, the electrocardiogram seldom shows signs diagnostic of myocardial necrosis. This is explained by the fact that in left bundle branch block, the initial vectors of ventricular activation are fundamentally altered in direction and the septum is depolarized in a direction opposite to the normal, i e, from right to left, causing an abnormal, initial positivity in the left ventricular cavity. Thus, it is impossible to diagnose a necrosis of the free wall of the left ventricle because the cavity potentials are transmitted to the epicardial surface through the "electrical window" and r waves are re-

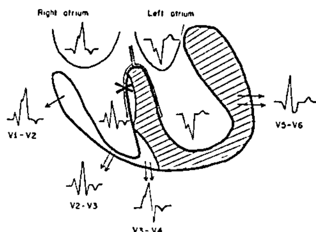


Fig. 11-25. Intracavitary and epicardial potentials in right bundle branch block.

third cardiac vector, which is the second septal vector This is demonstrated by the fact that the notching of the epicardial R′ is simultaneous with the peak of the intracavitary R′ (Fig. 11-23C, D). Finally, the peak of the epicardial R′ marks the arrival of the wave of excitation on the surface of the right ventricle and corresponds to the right intracavitary s wave. In other portions of the right ventricle corresponding to precordial leads V_3 and V_4, RS complexes are obtained with a notch on the ascending limb of the R wave This deflection is also partially due to low septal vectors located in the right portion of the septal mass, since this configuration cannot be explained on the basis of the above four vectors This has been emphasized by Sodi Pallares, who called attention to the fact that these R waves disappear in infarctions of the lower part of the septum

Over the epicardium of the left ventricle, qRS complexes are recorded, the initial negative deflection is due to septal activation from left to right, the R wave represents the activation of the free wall of the left ventricle (vector 2), and the S wave is generally widened and slurred, corresponding to vectors 3 and 4, which point away from the exploring electrode

In right bundle branch block, as shown above, the main abnormalities are those of the *late vectors*, which explains the slurring at the end of the QRS complexes in lead I and left precordial leads and the late R in aVR and in the right precordial leads, since the first vectors are directed from left to right, as in normal individuals, the q waves are present in lead II and over the left precordium, whereas the right precordial leads usually show an initial positive deflection.

On the basis of these data, the configuration of the various leads in right bundle branch block is easily understood

STANDARD LEADS. The QRS complexes show (Fig. 11-28A) notching and slurring with a duration of 0.12 sec or more, a widened S wave in lead I, usually smaller than the preceding R wave, is one of the main characteristics of this type of block; the q wave is usually present in this lead but may not be observed in certain cases. In lead III, the main deflection of the QRS complex varies according to cardiac rotation, it is negative in the horizontal hearts and positive in the vertical hearts. Several associated factors may change the configuration of the right bundle branch blocks in standard leads, particularly ventricular hypertrophy, myocardial disease, and the electrical position of the heart On the basis of the variations in configuration of the QRS complex in these leads, Bayley and Wilson et al. (1932) described several varieties of right bundle branch block which were subsequently thought to have different prognostic implications (Willius et al, 1941)

From a practical standpoint, the most common variety of right bundle branch block is the so-called *Wilson type of block* or *wide S_1 variety* It is characterized in lead I by a small initial q wave followed by a distinct, narrow R wave and a wide slurred S wave, with a positive T wave. In lead III, there is an rS complex or a deep Q wave with upright T in the horizontal heart, whereas in the vertical heart, the main QRS deflection is positive in lead III and is followed by a negative T wave. This variety of right bundle branch block is found in several types of heart disease, especially in chronic coronary insufficiency, but it may also occur in apparently normal individuals

The so-called *rare type of right bundle branch block* shows a small r in lead I (which may be absent in some cases), followed by a deep and wide S wave, while in lead III, the main QRS deflection is positive. The T wave in these leads is in the opposite direction of the QRS complex This type of right bundle branch block is often seen in right heart disease, suggesting the association of right bundle branch block with right ventricular hypertrophy.

A relatively rare variant of the Wilson type of right bundle branch block is the so-called *concordant inverted type*, in which wide S waves are present in the three standard leads (S_1, S_2, S_3)

Another type of right bundle branch block shows a wide, notched R wave in lead I, with or without an S wave and left axis deviation; the precordial leads are typical of right bundle branch block This type is not rarely encountered in cases of arteriosclerotic heart disease, but is especially common in Chagas' disease (Benchimol et al, 1954), where right bundle branch block is an exceedingly frequent finding However, vectorcardio-

D1

V

D2

D3

V

V

V

V

D2

V

D2

V5

Fig. 11-31. Electrocardiogram of a 67-year-old female with hypertensive and arteriosclerotic heart disease and angina pectoris of 2 years' duration. Note the initial complexes in each lead showing a normal intraventricular conduction This was obtained by a slight slowing of the cardiac rate as a result of ocular compression. The last QRS complexes in every lead exhibit a configuration of complete left bundle branch block In lead II, ventricular premature beats with a bigeminal rhythm are recorded.

corded instead of the typical Q waves which denote infarction. However, in the early stages of the coronary attack, the diagnosis of myocardial infarction associated with left bundle branch block may be suggested by ST-T and T-wave changes due to injury and ischemia, especially in cases that have a suggestive clinical history and in the presence of serial tracings.

When the infarct involves the *septal mass*, the initial negativity of the right ventricular cavity is transmitted to the left and is recorded through the infarcted area in left precordial leads, and occasionally in lead I. Thus, the presence of a Q wave in leads I, V_5, and V_6 in a case of left bundle branch block usually denotes an associated *septal infarction* (Fig 11-33D). The observation of RS complexes in leads V_5 and V_6 was suggested as a sign of *lateral wall infarction* in cases of left bundle branch block because of the recording of left intracavitary potential (RS) over the epicardial surface of the left ventricle through the area of myocardial necrosis (Fig. 11-30). It must be emphasized, however, that this configuration may also be recorded at the transitional zone if the latter is displaced to the left, as in a horizontal heart with a clockwise rotation.

It should be emphasized that Q waves may be present in leads I, V_5, and V_6 in cases of left bundle branch block without myocardial infarction. There are several possible interpretations for these initial negative deflections. (1) recording of left atrial potentials in horizontal hearts with marked clockwise rotation; (2) associated right

graphic studies seem to indicate that these cases correspond to left bundle branch blocks associated with extensive septal and inferolateral infarctions The standard leads in right bundle branch block also show secondary changes of the repolarization process, with asymmetric T waves in the opposite direction of the major deflection of the QRS complex, thus, they are usually positive in lead I, in view of the marked widening of the S wave, and negative in lead III The electrical axis of the T wave (AT) is usually deviated to the left, as opposed to the right axis deviation of the QRS complex.

UNIPOLAR LIMB LEADS The configuration of aVL and aVF varies according to the electrical position of the heart, although in aVR there is always a late, slurred R wave (Fig 11-28A). This deflection is due to the late activation of the right ventricle from left to right, upwards and anteriorly (vector 4), in the direction of the right arm The QRS complexes are similar to those obtained in the right atrial cavity, whereas those of aVL and aVF resemble the left ventricular epicardial leads

PRECORDIAL LEADS In the right precordial leads (V_1 and V_2), the ventricular complexes are usually of the rsR' type with variations in the amplitude of the deflections from one case to another, involving particularly the first two waves of the QRS complex Occasionally, the S wave does not reach the base line and the configuration becomes rR' *The peak of the R' wave corresponds to the arrival of the wave of excitation over the right ventricular epicardial surface and is always delayed* Very often, there is a notch on the ascending limb of R' which marks the end of septal activation and the beginning of depolarization of the free wall of the right ventricle (Fig 11-23C, D), this was demonstrated by simultaneous recordings of precordial and right ventricular intracavitary leads

Since the beginning of septal activation is unchanged in right bundle branch block and is directed from left to right, the QRS complexes are almost always initially positive However, the absence of an initial r wave in V_1 does not necessarily represent an associated anteroseptal necrosis, it may be due to either a perpendicular direction of the first vector to lead V_1, or an enlarged right atrium which transmits its potential to lead V_1

With reference to ventricular repolarization, secondary inversion of the T wave is often seen, with a depressed S-T segment in leads V_1 and V_2

In the left precordial leads (V_5 and V_6), the QRS complexes are usually of the qRS type, similar to lead I, with a wide and slurred S wave (Fig 11-28A) In the absence of an associated left ventricular hypertrophy, there is no delay in the intrinsicoid deflection The T waves are generally positive, if they are negative, this suggests myocardial ischemia or left ventricular hypertrophy.

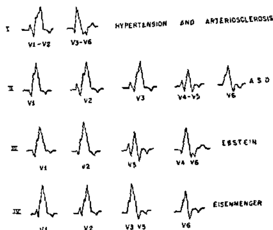


Fig. 11-26. Right bundle branch block in various types of heart disease (precordial leads).

In the intermediary points over the precordium (between leads V_1 and V_2), it is not unusual to record QRS complexes which resemble those of the right intracavitary leads (rsR'S'), probably corresponding to the thin trabecular zone of the free wall of the right ventricle In leads V_3 and V_4, an RS configuration is frequently obtained with a notch on the ascending limb of the R wave These waves are probably due to the low septal vectors pertaining to the right ventricular portion of the septum, as previously described (Fig. 11-25)

In the following types of heart disease with right bundle branch block, certain configurations of the precordial leads are often of diagnostic importance (Fig. 11-26):

1 In *arteriosclerotic* and *hypertensive heart disease* it is not unusual to record qRS complexes from leads V_3 to V_6, suggesting that the potentials of the hypertrophied left ventricle are transmitted to all leads which are to the left of V_3

2. In *atrial septal defect* (ASD), qR complexes are often obtained in lead V_1, because of right atrial enlargement, whereas the remaining precordial leads (V_2 to V_6) show right ventricular potentials, initially (V_2 and V_3) according the potential variations or the free wall, then those of the trabecular zone (V_4 and V_5), and finally those of the right side of the septum (V_6).

3. In *Ebstein's disease*, the potentials of the right atrium (qR) are recorded in leads V_3R, V_1, V_2 and occasionally extend to other precordial leads The left ventricular potentials

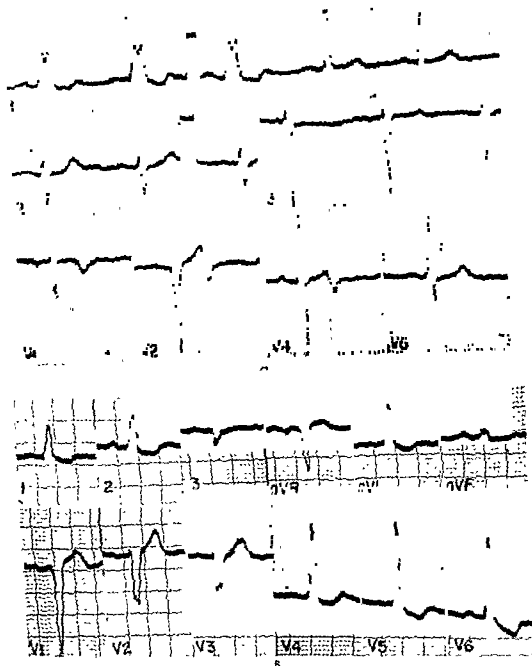


Fig. 11-32. A *Left bundle branch block. Note in lead I a transitional complex with the configuration of incomplete left bundle branch block, followed by a QRS complex with normal intraventricular conduction (the last complex in lead I). In the remaining leads the ECG shows incomplete left bundle branch block.* B *Second-degree incomplete left bundle branch block in a 65-year-old patient with hypertensive and arteriosclerotic heart disease*

(qRS) are recorded in leads V_4 to V_6. Only occasionally are the right ventricular potentials obtained from the trabecular zone in lead V_3. Thus, in Ebstein's disease, the dominant electrocardiographic signs are those due to the right atrium and left ventricle, with a limited area of right ventricular complexes over the precordium.

4. In *Eisenmenger's syndrome*, leads V_3 to V_6 reflect the potential variations of the lower part of the septum, whereas leads V_1 and V_2 record rsR′ complexes from the free wall of the right ventricle. Left ventricular configurations (qRS) are occasionally seen in lead VF.

Complete Left Bundle Branch Block. *When the left branch of the bundle of His is incapable of transmitting the cardiac stimulus, the entire septum is activated from right to left and the initial vectors become definitely abnormal. As a result, the q wave disappears in all leads which reflect the potentials of the left ventricle. In addition, there are an increased duration and a change in configuration of the QRS complexes, which become widened, slurred, and notched*

These abnormalities can be attributed to the three main points of delay in the spread of the stimulus throughout the septal mass, as previously discussed with reference to cardiac activation in left bundle branch block.

A comparison of the unipolar epicardial configuration with the intracavitary leads is important in order to understand and interpret the standard and precordial leads. According to the experimental work of Sodi Pallares et al. (1950), in the intracavitary lead of the *left* ventricle, the form of the QRS complex varies from one point to another, in the lower part of the cavity, RS complexes are obtained, whereas the upper posterobasal portions show a qR configuration. The presence of a q wave in those leads is presumably due to the first septal vector, which is oriented from right to left, downwards, and slightly anteriorly; it is also possible that the lower part of the right aspect of the septum may contribute toward this deflection. This configuration is important for the diagnosis of infarcts involving the middle third of the septum, since in these cases, instead of RS complexes in the lower part of the left ventricular cavity, the tracing shows qR deflections resembling those of the posterobasal intraventricular leads. The S wave, which may be recorded in the cavity of the *left* ventricle, is probably due either to the activation of the upper part of the septum or to that of the free wall of the left ventricle.

In the cavity of the *right* ventricle, the configuration of left bundle branch block is essentially negative (QS), with notching and slurring of the QRS complexes.

Certain aspects of the epicardial leads in relation to the intracavitary potentials need further discussion (Fig. 11-27A). In the epicardial leads over the right ventricle, the R waves are often absent from V_1 to V_4, in view of the fact that the right-to-left septal vector is of great magnitude and neutralizes those of the free wall and the lower septal portion of the right ventricle. In the leads over the left ventricle (V_5 and V_6), the ascending limb of the R wave is probably due to the spread of the stimulus through the barrier, whereas the slurring of the "plateau" of the QRS complex corresponds to the activation of the septum from right to left; finally, the last peak of the

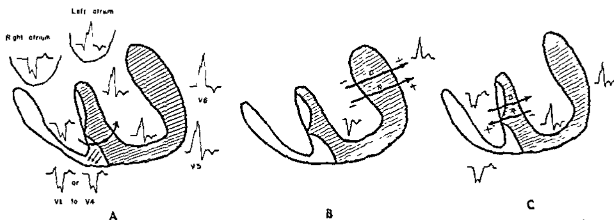


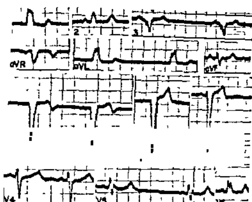
Fig. 11-27. A. Intracavitary and epicardial potentials in left bundle branch block. B. Ventricular repolarization in the normal heart. C. Ventricular repolarization in left bundle branch block.

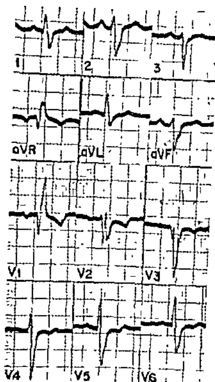
ventricular hypertrophy; (3) right intraventricular conduction defect (Laham, 1952).

Certain cases of left bundle branch block show Q waves in leads I, V_5, and V_6 *in the* absence of myocardial infarction. This is because of one of the following possibilities: (1) recording of left atrial potentials over the pre*cordium in* horizontal hearts with marked clockwise rotation; (2) associated right ventricular hypertrophy; or (3) right intraventricular conduction defects.

Cabrera and Friedland (1953) called attention to the importance of a late notching of the S or QS wave in leads V_3 and V_4 as a strong indication of myocardial necrosis in the









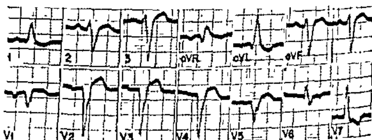


Fig. 11-33. A. Complete left bundle branch block in a 42-year-old patient who was asymptomatic and showed a normal heart size on roentgenologic examination B. Right bundle branch block and anteroseptal infarction C in a 45-year-old patient. D Complete left bundle branch block and anterior wall infarction with septal involvement, recorded during the acute and subacute stages of coronary occlusion. Observe ST-T changes and the deep Q waves in leads I, aVL, and V_6 indicating myocardial necrosis E Left bundle branch block and anterior wall infarction showing a late notch on the ascending limb of the S waves in leads V_2 to V_4. This case had autopsy confirmation.

R wave is due to the depolarization of the free wall of the left *ventricle*. *Actually*, it is not known exactly where the septal activation ends and that of the free wall of the left ventricle *begins*

STANDARD LEADS. *The QRS complexes* are notched, slurred, and widened, with a *duration* of 0 12 sec or more (Fig. 11-28B) There are *no q or S waves* in lead I, and the mean electrical axis of the QRS complex (ÂQRS) is deviated to the left from 0 to −75°. *In rare cases*, the electric axis is within normal *limits, and under unusual* circumstances, a right axis deviation may be present

The presence of a q wave in lead I would suggest a previous septal infarction, peri-infarctional block, *respiratory* variations of cardiac position, or other factors, including right ventricular hypertrophy

The variations of ÂQRS in left bundle branch block are due to several factors, such as left ventricular hypertrophy, the location and extension of *coexistent* myocardial lesions, and especially the position of the heart to the chest. *The concordant* types and those with right axis deviation are generally found in *vertical hearts*

The T waves are asymmetric and opposed to the major deflection of the QRS *complex, this is* also observed *with reference to the S-T segment*

UNIPOLAR LIMB LEADS *The* patterns obtained in these leads are essentially dependent upon the electrical position of the heart Since left bundle branch block is mostly seen in *horizontal hearts*, lead aVL records left ventricular potentials *and* is similar to leads I, V_5, and V_6 *In some of these cases, a small q wave may be recorded in these leads in the absence of anteroseptal infarction* In lead aVF, the ventricular complexes are of the rS or QS types, a fact which is *not* due to myocardial necrosis. Lead aVR shows variable configurations (rS, QS, QR), *according to the position* of the QRS axis, and generally resembles the right atrial intracavitary lead

In the *unusual* cases occurring in *vertical hearts*, aVF records left ventricular potentials and aVL faces the right ventricle, whereas aVR is variable and depends upon the degree of right axis deviation This electrical position is *responsible for* patterns simulating *right bundle* branch block in the standard leads, although the precordial configurations *are typical* and diagnostic

PRECORDIAL LEADS. In leads V_5 and V_6 corresponding to the left ventricle, essentially positive *QRS* complexes are obtained with an initial, *slurred* R wave of variable amplitude *(Fig 11-28B)* Following this deflection, *there is always* a notched plateau which *extends to the peak* of a rapid and delayed *intrinsicoid* deflection; in certain cases, these complexes assume an *M-shaped configuration* There is, as yet, no complete agreement as to the correct interpretation of the plateau.

It is *to be emphasized* that in hearts with marked *clockwise rotation, these* QRS complexes are observed *only* in lead V_7 (or *farther to the* left), which may suggest an associated right ventricular enlargement. The T waves are negative, *with an S-T* segment depression and an upward *concavity of the S-T segment*; these repolarization changes are secondary to the QRS *abnormality*.

In leads over the right ventricle (V_1 and V_2), the tracing does not show remarkable changes, as it begins with a small r wave and ends with a wide and deep S wave. *The persistence of the initial r wave in the left bundle branch block*, in the presence of an inverted septal activation, is probably explained by early activation of the free wall of the right ventricle, in addition to that of *the lower portions of the septum pertaining to this ventricle. Very often*, however, this small *r* wave disappears, and QS complexes *are recorded* in the right precordial leads, suggesting the presence of anteroseptal infarction. In these cases, the negativity *is explained by a neutralization of the lower septal vectors and those of the* free wall *by the more* powerful septal forces directed from right to left. The T waves are positive in these leads, with elevated S-T segments.

Ventricular Repolarization in Left Bundle Branch Block. Under normal circumstances, the *repolarization process of the* free wall of *the left ventricle* dominates that of the interventricular septum, and explains the negative T wave in the ventricular *cavity with an upright* deflection over the epicardial surface. This is because, in man, repolarization proceeds in an opposite direction to that of *depolarization* (Fig 11-27C *and D*). *In left* bundle branch block, septal repolarization is greater than that of the free wall and is directed from right to left, although the *vector is conventionally represented in the opposite* direction This explains the negative T wave both in the cavity and over the left ventricular *epicardium. Consequently, septal repolarization is mainly responsible for the* T wave changes in left bundle branch block.

INCOMPLETE BUNDLE BRANCH BLOCK

The concept of "incomplete" bundle branch block presupposes a delay in *conduction* through one of the *branches of the His* bundle, although the *excitation wave* is not entirely

presence of left bundle branch block (Fig. 11-33E).

Sodi Pallares et al. (1957) described eight varieties of infarction complicated by bundle branch block, which could be distinguished electrocardiographically on the basis of the modern concepts of ventricular activation and the identification of the intracavitary potentials. It was shown by these authors th [illegible] involvement [illegible] block, could be suggest [illegible] tary potentials (RS) in precordial leads V_5 and [illegible] be possible to [illegible] ment and in cases with extension into the [illegible] wall of the left ventricle.

Most pathologic studies have confirmed the electrocardiographic criteria for the diagnosis of myocardial infarction complicated by left bundle branch block.

THE VECTORCARDIOGRAM IN BUNDLE BRANCH BLOCK

Vectorcardiography has unquestionably played an important role in the better understanding of many obscure aspects of the ECG, particularly with reference to the intraventricular conduction defects

Nevertheless, the subject of conduction defects has not yet been completely clarified, and there are still many controversial opinions regarding electrogenesis and the correct interpretation of many ECG tracings, as well as VCG loops. Adequate experimental data, in addition to electrovectorcardiographic correlation, are still lacking Lately, however, important contributions have been published in the literature on this subject, and many problems have appeared requiring future investigation.

The VCG is very useful in the diagnosis of the more advanced forms of bundle branch block. Interpretation of the lesser degrees of these conduction defects is still controversial, and, at present, it is difficult to distinguish certain cases of ventricular hypertrophy from the so-called incomplete types of bundle branch block.

As previously mentioned, the electrocardiographic diagnosis of bundle branch block is based upon certain findings, such as atrioventricular conduction, abnormal slurring and notching of the QRS complexes, and a late R wave in the unipolar leads facing the ventricle on the side of the blocked bundle branch.

Atrioventricular conduction cannot be demonstrated in the VCG, it is necessary to record the ECG for this purpose. With reference to notching and slurring, the VCG is a more adequate tracing, since it distinguishes the true from the false types of slurring True slurring is due to a slow inscription of the spatial vectors, and it is observed in the various planes, the false types of slurring result from the perpendicularity of certain portions of the VCG loop in relation to one of the planes, and are therefore limited to this plane.

Finally, the late R wave corresponding to the ventricle with delayed activation is shown in the VCG by a loop which points toward this ventricle As a rule, the main vectorcardiographic features of bundle branch block are the slow inscription of certain portions of the loop, the direction of the initial part of the loop, and frequently the type of rotation in the horizontal plane (Grishman and Scherlis, 1952).

In Complete Left Bundle Branch Block. The main VCG features of complete left bundle branch block are as follows (Fig. 11-34).

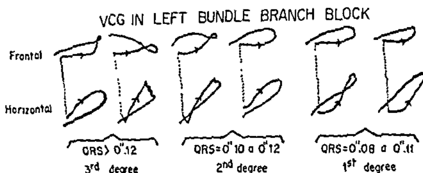


Fig. 11-34.

arrested as in the "complete" types of block. Thus, the activation of each ventricle in the incomplete bundle branch blocks proceeds through its corresponding branch, though with a variable degree of delay.

This interpretation was accepted following the investigations of Wilson and Herrmann, which were later confirmed and extended by Sodi Pallares (1950), in addition to the clinical observation of tracings similar to those experimentally obtained

The fact that both clinically and experimentally, continuous tracings were obtained showing QRS complexes intermediate in configuration between normal records and complete bundle branch block (Fig 11-32A) seems to confirm the actual existence of incomplete bundle branch block, which has been such a controversial subject among the various investigators.

From the morphologic standpoint, these tracings resemble complete bundle branch block, although the duration of the QRS complexes is less than 0.12 sec (usually between 0.10 and 0.12 sec). However, Sodi Pallares attaches greater importance to the morphologic

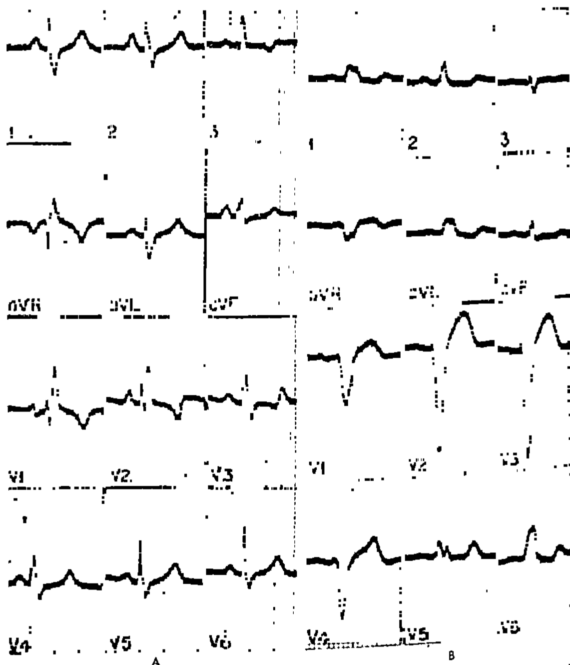


Fig. 11-28. A. Complete right bundle branch block in a 29-year-old patient with interatrial septal defect B. Complete left bundle branch block in a 60-year-old patient with arteriosclerotic heart disease.

1. Changes in the spatial QRS loop. In the *horizontal plane,* the initial portion of the loop (Q loop) decreases, and is slowly inscribed, oriented usually forward and slightly to the left; in some cases, however, it is directed posteriorly and to the left, and very rarely anteriorly and slightly to the right. Whatever its initial direction, the QRS loop, sometimes after a sharp angulation, is rapidly inscribed posteriorly and to the left (R loop) with a clockwise rotation, which is the main VCG feature of this type of block.

The long axis of the loop usually lies between −30 and −60° in the horizontal plane. In the afferent limb, or more frequently in its middle portion, there is evidence of conduction delay, as shown by the closer proximity of the time markings. At this point, there is an irregularity of the loop, constituting a "plateau," the duration of which is proportional to the degree of block (Fig. 11-35).

Occasionally, the VCG in the horizontal plane is characterized by a "figure-8" type of rotation, with an initial counterclockwise direction followed by a clockwise inscription; in these cases, the Q loop is usually directed anteriorly and to the left.

The QRS sÊ usually fails to close prior to the inscription of the T sÊ loop, this is because it does not return to its point of origin, so that the J point is deviated to the right and anteriorly, resulting in an ST vector pointing in the same direction.

In the *frontal plane,* the QRS sÊ loop of the VCG is inscribed counterclockwise (with very rare exceptions), to the left, and superiorly. The loop is usually open, with an ST vector pointing downward and to the right.

In the *sagittal plane,* it is important to note the clockwise rotation of the loop, with its main axis pointing posteriorly and slightly superiorly or inferiorly. The loop fails to close as in the other planes, with an ST vector pointing anteriorly and slightly inferiorly.

2. Spatial T Loop (T sÊ). The T sÊ loop is usually oriented opposite the QRS sÊ loop, to the right, anteriorly and superiorly or inferiorly.

In Incomplete Left Bundle Branch Block. The vectorcardiographic criteria of incomplete left bundle branch block are much less precise

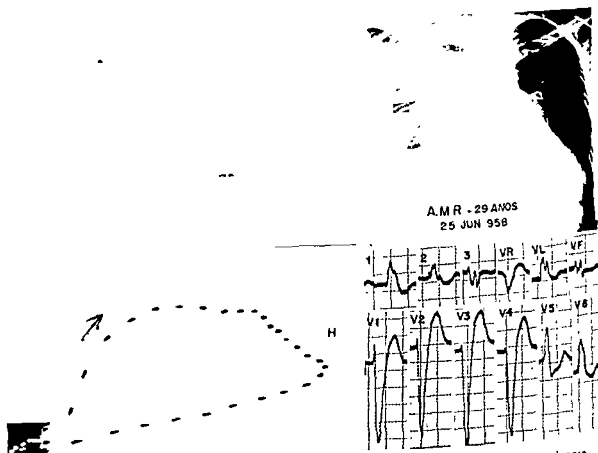


Fig. 11-35. Complete left bundle branch block in a 29-year-old male with Chagas' heart disease. The VCG shows the typical clockwise rotation in the horizontal plane with a delay in the middle portion of the loop.

criteria than to the delay of the intrinsicoid deflection, accepting as incomplete bundle branch blocks even cases with a normal QRS duration (less than 0.10 sec).

Incomplete Right Bundle Branch Block. This type includes electrocardiograms with an rsR' configuration in the right precordial leads, with variable amplitudes of the individual deflections, and a total duration of the QRS complexes below 0.12 sec. Although the intrinsicoid deflection is inscribed with a delay of 0.04 to 0.06 sec, the marked delay observed in incomplete right bundle branch block is not seen in these cases. In the standard leads, the tracing may be normal, although there often is a slurred S wave in lead I and a late wide R wave in lead III.

This type of electrocardiogram is frequently observed in normal individuals, although it is especially common in diseases affecting the right heart (atrial septal defect, tricuspid insufficiency, etc.). Although Sodi Pallares et al. (1950) consider this configuration as due always to a right bundle branch conduction defect, Kossmann et al. (1950) admit the possibility of a late activation of the crista supraventricularis of the right ventricle, both in normal individuals and in some persons with right ventricular hypertrophy.

From a practical standpoint, it is obvious that not all tracings with this configuration actually represent incomplete right bundle branch block. However, it is extremely difficult to distinguish the true incomplete right bundle branch block from similar tracings which correspond to normal variants, or those due to right ventricular hypertrophy, although several criteria have been suggested to differentiate these conditions. The most important practical contribution to this problem has been that of vectorcardiography in clarifying certain aspects of the rSR' configuration in V_1.

Incomplete Left Bundle Branch Block (Fig. 11-24). The *first-degree left bundle branch block* is characterized by an absence of q waves in leads V_5 and V_6, which is not in itself sufficiently diagnostic, since this may occur in normal individuals with vertical heart and a clockwise rotation. However, the presence of an initial slurring of the R wave in these leads is of greater diagnostic importance, since it represents bilateral septal forces which neutralize each other. The T waves are either normal or slightly decreased in amplitude.

In *second-degree left bundle branch block*, septal activation is partly inverted, the majority of the septal mass being activated from right to left. Only a small portion of the left side of the septum is activated by late forces directed from left to right. In these cases, Q waves are absent in leads V_5 and V_6 and there is a slurring of the entire upstroke of the R wave. The duration of the QRS interval is slightly greater than that of first-degree bundle branch block, and the T wave becomes negative because of the inverted direction of septal repolarization (Fig. 11-32B).

In contrast to the incomplete right bundle branch block, which may occur in normal hearts, in the majority of cases, incomplete left bundle branch block denotes organic heart disease with left ventricular hypertrophy. The occurrence in continuous tracings of complete and incomplete left bundle branch block alternating with a normal QRS complex constitutes important evidence in favor of the incomplete bundle branch block concept, which is still denied by some authors.

BUNDLE BRANCH BLOCK AND VENTRICULAR HYPERTROPHY

The configuration of *right bundle branch block*, especially of the incomplete type, is often seen in certain types of right heart disease, such as atrial septal defects, tricuspid insufficiency, etc., and has been described by Cabrera and Monroy as evidence of *diastolic overload of the right ventricle.* Although this is true in most cases, it should be emphasized that similar electrocardiograms may be observed in normal hearts and in cases of true right bundle branch block. The distinction between these three conditions is difficult from an electrocardiographic standpoint, and it is often necessary to base the interpretation upon clinical data and on other abnormalities of the tracing (P pulmonale, Lewis index, right axis deviation, etc.). *Vectorcardiography* is of great help, because the orientation of the loop in the horizontal plane is frequently diagnostic and differs in right ventricular hypertrophy from that in normal hearts and in right bundle branch block.

It is well known that *left bundle branch block* usually coexists with left ventricular hypertrophy. According to most authors, the latter is practically inferred in the presence of this type of conduction defect; however, there are

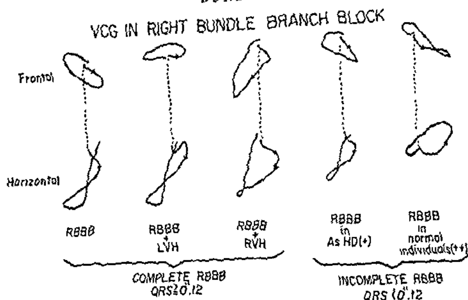


Fig. 11-36.

than those of the complete type. Very often, the VCG in incomplete left bundle branch block is similar in configuration to that of complete left bundle branch block, with the exception of its duration (less than 12 sec) and the lesser degree of slowing observed in the middle portion of the loop (first- and second-degree left bundle branch block) (Fig 11-34).

In certain instances, the slowing of the middle portion does not occur, but the loop is inscribed in a clockwise direction in the horizontal plane; this is an important distinguishing feature from simple left ventricular hypertrophy.

The QRS sE loop in the horizontal plane is frequently inscribed to the left and posteriorly, initially with a counterclockwise rotation, followed by a clockwise rotation which may occur at different points of the loop, near its middle portion or not. In these cases, the loop has a characteristic figure-8 type of configuration with a slow inscription of its initial portions, with or without an additional delay in the middle portion of the loop.

Finally, in certain instances of incomplete left bundle branch block, the middle portion of the horizontal QRS loop shows either a slight slurring or a counterclockwise rotation, although a certain delay in the initial portion of the loop is observed, it is difficult to distinguish these types of VCG from those of left ventricular hypertrophy.

In Right Bundle Branch Block. The initial portion of the QRS sE loop is normally inscribed, i e, to the right and anteriorly, since the initial vectors of ventricular activation remain unchanged in this type of conduction defect. The most important feature of the loop is its terminal portion, which is slowly inscribed, with an irregular contour constituting an appendage, which in the horizontal plane is directed anteriorly and to the right (Fig 11-36) The general aspect of the loop varies in form and direction.

Two main types have been pointed out One was described by Grishman et al. (1938), with a QRS sE loop inscribed to the left and posteriorly and a counterclockwise rotation in the horizontal plane followed by a delayed terminal appendage [Fig. 11-36(1)]. These loops correspond to the ECGs of the so-called atypical forms of right bundle branch block, and are often found in chronic Chagas' heart disease, AV communis, and other cardiac conditions. A second type of VCG in right bundle branch block has been emphasized by Cabrera et al. (1958), with the QRS sE loop in the horizontal plane showing an initial clockwise rotation,

a few exceptions to this rule, such as the case shown in Fig. 11-24B.

In the presence of associated bundle branch block, the classical electrocardiographic criteria for the diagnosis of ventricular hypertrophy may not apply, because of the altered pathways of ventricular activation. In such instances, the recognition of ventricular overload may be extremely difficult.

A review of the criteria proposed by a number of authors, which so far have been accepted, has shown that they cannot be used in many cases.

Many of these patterns appear in *experimental blocks*, and occasionally in a variety of clinical cases, in which the diagnosis of coexistent ventricular hypertrophy cannot be made unequivocally. On the other hand, certain cases of *transient bundle branch block* with suggestive evidence of associated hypertrophy have not exhibited any of the diagnostic criteria of ventricular overload following the restoration of normal conduction.

At present, it appears that the best criteria for the diagnosis of ventricular hypertrophy associated with bundle branch block are the following.

1 *Diagnosis of right ventricular hypertrophy in the presence of right bundle branch block*

a. Signs of right atrial enlargement

b. Right axis deviation exceeding +120°

c. Presence of RR′ in leads to the left of V_3 (this is considered as evidence of right ventricular dilatation)

d. Deeply inverted T waves in V_1, V_2, and V_3

Although, from a statistical standpoint, deep S waves in leads I, V_5, and V_6, or an R′ exceeding 10 mm in V_1, occur more frequently in cases of associated right ventricular hypertrophy, these signs may also make an appearance in many cases of isolated right bundle branch block.

2. *Diagnosis of left ventricular hypertrophy in the presence of right bundle branch block*

a. Signs of left atrial enlargement (in the absence of mitral stenosis)

b. R waves of high voltage and a delayed intrinsicoid deflection in V_5 and V_6 (0.05 sec)

c. Deep S wave preceding an R′ in V_1 and V_2

d. QRS axis deviated upwards and to the left in the frontal plane

e. Presence of q waves in leads I, V_5, and V_6

Other minor signs, which may be useful in some cases, are the early transition in the precordial leads and the presence of T-wave inversion in leads V_5 and V_6

3. *Diagnosis of left ventricular hypertrophy in the presence of left bundle branch block*

As previously stated, the presence of left bundle branch block in itself is considered evidence of associated left ventricular hypertrophy in view of the high statistical incidence (approximately 95 per cent) of left ventricular enlargement in cases of left bundle branch block. Nevertheless, the following signs are highly suggestive of left ventricular hypertrophy in the presence of left bundle branch block:

a. Sokolow-Lyon index above 35 mm

b. White-Bock index above +18 mm

c. Marked left axis deviation of the QRS complex, with right axis deviation of the T wave

d. Tall R waves in the left precordial leads with a tendency to the disappearance of the "plateau"

e. Signs of left atrial enlargement (an indirect sign, although one of the most important diagnostic criteria of associated left ventricular hypertrophy)

Under these circumstances, it is very difficult to identify right ventricular hypertrophy for several reasons, including the fact that these cases usually exhibit biventricular hypertrophy associated with left bundle branch block.

However, vertical electrical position of the heart, clockwise rotation, and leftward displacement of the transitional zone in precordial leads with S waves in V_6 and V_7 are highly suggestive of coexistent right ventricular hypertrophy (Laham, 1951, 1952).

From a *vectorcardiographic* standpoint, the association of right ventricular hypertrophy and right bundle branch block has been described (Burch et al., 1953, Wolff et al., 1953) as showing a displacement of the QRS loop anteriorly and to the right and as maintaining the classical VCG characteristics of right bundle branch block (delayed terminal appendage) [Fig. 11-36(2)]

Left ventricular hypertrophy in right bundle branch block displaces the loop so that it as-

followed by a counterclockwise inscription, and a preterminal delay often resulting in a figure-8 configuration [Fig. 11-36(2)]. This type is often seen in coronary heart disease.

The T loop is usually opposed to the delayed terminal appendage, and its abnormalities are less conspicuous than those of left bundle branch block. The vectorcardiographic distinction between *complete* and *incomplete right bundle branch block* is made solely on the basis of the duration of inscription, since there are no significant differences in configuration of the respective VCG loops.

The VCG has been found to be the most useful in distinguishing incomplete right bundle branch block from other tracings with an rsR′ configuration in lead V_1, which correspond to either normal hearts or slight degrees of right ventricular hypertrophy.

ETIOLOGY

Coronary heart disease is undoubtedly the main cause of bundle branch block, either as an isolated factor or in association with arterial hypertension. One of the branches may be damaged by an *acute infarction*, followed by fibrosis, or by a slow and progressive *ischemia* due to chronic coronary insufficiency.

Bundle branch blocks may be found in the absence of any type of apparent organic heart disease; this is much more common in right than in left bundle branch block.

Left bundle branch blocks occur mostly in hypertensive or arteriosclerotic heart disease and in aortic valvular disease, especially in *calcific aortic stenosis* and in *syphilitic aortic insufficiency*. Less common causes are classified in Table 11-2.

Right bundle branch blocks are observed in normal persons and in a variety of organic heart diseases, and are thus commonly found in clinical practice.

In normal individuals, right bundle branch block is usually of the incomplete type, decreasing during the Valsalva maneuver and increasing during the Muller maneuver. The elec-

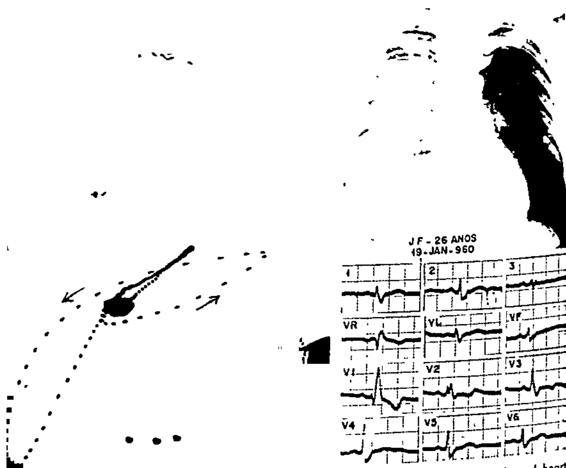


Fig 11-36(1). Complete right bundle branch block in a 26-year-old patient with Chagas' heart disease. The mean spatial QRS axis is at −150°. The VCG shows a counterclockwise rotation in the horizontal plane, with a terminal delayed appendage pointing rightward and anteriorly.

sumes a more superior orientation as compared with its position in uncomplicated right bundle branch block (Grishman and Scherlis, 1952; Burch et al., 1953; *Massie and Walsh*, 1960).

An interesting type of left ventricular hypertrophy with terminal delay in intraventricular conduction has been described by Grishman and Scherlis (1952). In these cases, the ECG displays a widened QRS complex, with wide, slurred S waves in V_6, marked left axis deviation, and secondary S-T segment and T-wave changes.

The VCG in these cases shows the typical signs of left ventricular hypertrophy, with a delay in the terminal segment of the afferent portion of the QRS loop, which is oriented to the right, posteriorly, and superiorly.

INTERMITTENT BUNDLE BRANCH BLOCK

Experimentally, a complete bundle branch block pattern may be obtained by direct percussion of one of the branches of the bundle of His (this is more easily obtained in the right bundle branch), and serial changes of the tracing are recorded. It is interesting to note then that as the conduction defect improves, the degree of block progressively decreases until normal conduction is finally restored. It is conceivable, therefore, that *in the presence of* an organic lesion of one of the branches of the bundle of His, the occurrence of an attack of tachycardia, or any other aggravating factor of the conduction defect, may lead to a transient block of the impulse through the damaged bundle branch. Thus, intermittent bundle branch blocks are probably more common than they appear to be statistically, and would probably be more frequently recorded if serial tracings were obtained in the initial stages of the organic bundle branch lesions. Nevertheless, numerous cases of transient bundle branch block have been published in the literature (Bénchimol, 1944, 1945), demonstrating that this is not a rare finding in clinical cases.

It was thought at first that this represented a purely *functional disturbance*; however, it is now considered to be due to lesion of the conduction tissues, frequently denoting advanced cardiac disease. The majority of the so-called "functional" bundle branch blocks is observed in the course of supraventricular tachycardia or atrial flutter or fibrillation. Although some patients with this type of block *do not appear to* suffer from any cardiac disease, it is difficult to rule out minor lesions of the conduction tissues leading to *fatigue of the bundle branch* with a decrease in its conduction capacity in the presence of a functional strain. Many factors have been *described as capable of* precipitating these types of block. Thus, changes of vagal tone or of heart rate, hypoxia, heart failure, toxic processes, etc., have been considered.

Although changes in vagal tone may indirectly influence intraventricular conduction, it appears that this increased tone is not directly t[illegible]sible for the prolonged inhibition of con-

[illegible]

[illegible] factor, have been described (Vessell, 1951). There was a critical rate for the appearance of block, and this often disappeared following a slight decrease of rate. In other instances, the bundle branch block appears on effort or following some factor which temporarily overloads the heart in the presence of advanced pathologic changes (usually due to coronary arteriosclerosis).

In these cases, *the different involvement of the two branches leads to a difference of their refractory periods.* However, a normal intraventricular conduction is still compatible with a permanent increase in the refractory period predominating in one of the branches of the bundle of His. The conduction defect only appears following the influence of certain factors, which increase the refractory period or inhibit conduction completely.

Cases have been described in which bundle branch block appeared in the course of heart failure and disappeared as soon as cardiac compensation was obtained. Other instances



Fig. 11-29. Electrocardiogram of a 65-year-old male with complete right bundle branch block and anterolateral infarction; deep Q waves are recorded in left precordial leads, with the *typical right bundle branch configuration maintained in leads* V_1 and V_2.

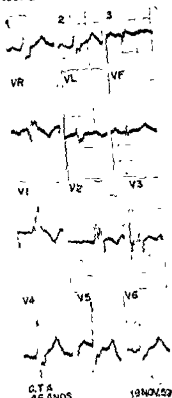


Fig 11-36(2). Right bundle branch block with ÂQRS at 180° in a 46-year-old patient. The VCG displays an initial clockwise rotation of the loop in the horizontal plane, followed by a counterclockwise rotation and a delay in the terminal portion

trocardiographic and vectorcardiographic features are usually similar to those found in *pectus excavatus* and in certain *atrial septal defects* without pulmonary hypertension.

In younger patients, the main causes of right bundle branch block are *congenital heart disease, rheumatic heart disease,* and *Chagas' disease.*

With reference to rheumatic heart disease, right bundle branch block is usually found in the presence of mitral and tricuspid lesions. In these instances, P-wave changes diagnostic of biauricular enlargement are usually present, or atrial fibrillation, in addition to other characteristic changes of rheumatic heart disease.

In *pure mitral stenosis,* which exhibits a double-peaked R wave in V_1, there is usually a moderate degree of right ventricular enlargement.

In many Latin American countries, a common cause of right bundle branch block is *chronic Chagas' heart disease,* which shows a remarkably high incidence of this type of conduction disturbance. The ECG usually records a complete type of right bundle branch block, with left axis deviation as a very common finding [Fig. 11-36(3)]. In serial tracings, other electrocardiographic abnormalities are often associated, such as ventricular premature beats and various types of AV block.

In congenital heart disease, right bundle branch block is frequently recorded (Table 11-3), especially in *atrial septal defects,* either as an isolated finding or associated with other cardiac malformations.

In isolated atrial septal defects, according to most authors, right bundle branch block is an evidence of *diastolic overload* of the right ventricle; in such instances, the conduction defect is either complete or, more frequently, incomplete, with right axis deviation, and, contrary to the situation in coronary cases, very seldom shows a counterclockwise rotation. The P-wave changes are usually more marked than those observed in coronary insufficiency, although of a lesser degree than those exhibited by mitrotricuspid patients.

The problem of right bundle branch block, and especially that of a double-peaked R wave in right precordial leads, is of great interest

tached at all. The septal leaflet may or may not be attached. The new "tricuspid orifice" may be small or large and may be normal functionally or the seat of an insufficiency or, less commonly, stenosis. There is usually a patent foramen ovale. The right atrium is hypertrophied and dilated. The proximal part of the right ventricle is dilated. The distal part of the right ventricle may be hypertrophied or normal in thickness. The left atrium and ventricle may be normal or hypertrophied. The pulmonary artery is usually small. Fibroelastosis is often present in the proximal right ventricular chamber. The conduction system may be normal, or accessory muscle bundles may bridge the right atrium and ventricle.

PATHOGENESIS OF THE COMPLEX. The displaced tricuspid orifice may be considered to be the basic anomaly. Thus, the right atrium and proximal part of the right ventricle act as a unit, although the exact method of their functioning is not clear. There is usually decreased pulmonary flow. If there is a functional tricuspid stenosis, then there is a venoarterial shunt at the atrial level, and hence the left atrium and ventricle may present a volume hypertrophy, if not counterbalanced by the decreased pulmonary flow.

Hypoplasia of the Aortic Tract Complexes. In this group (Lev, 1953) the following common denominators exist (Fig. 6-9A): (1) The aortic orifice, the ascending and the trans-





Fig. 6-8 Tricuspid atre... atresia B Right ventr... cuspid atresia, D, atri... ...ative right ventricle ...right ventricle T, tricuspid atrial and proximal right ventricular chamber. D View of tricuspid valve and conus RA, right atrium, Pr, proximal chamber, C, conus (C D. From M. Lev. Autopsy Diagnosis of Congenitally Malformed Hearts, Charles C Thomas, 1953.)

creased pulmonary flow. It appears that the total ventricular mass is greater than normal, but this is not certain.

Complete Transposition with Single Ventricle and Diminutive Outlet Chamber. In this anomaly (Taussig, 1938; Megevand et al.), the mitral and tricuspid orifices enter a single common chamber (Fig 6-7C). This chamber communicates by a variously sized opening with a smaller chamber situated humplike over the anterior wall of the main chamber. The aorta emerges from the diminutive chamber, while the pulmonary artery emerges from the main chamber Either vessel may be large or small, dependent upon size of the communication between the two chambers. The main ventricular chamber is a common ventricle, while the recess is produced by the crista supraventricularis forming a pseudoseptum.

PATHOGENESIS OF THE COMPLEX The basic anomaly may again be considered to be the position of the arterial trunks. Since the pulmonary artery is usually related to the large chamber, there is increased pulmonary flow.

Complete Transposition with Mitral and Tricuspid Atresia. This will be considered under mitral and tricuspid atresia

Corrected Transposition. In this anomaly (Cardell), the arterial trunks emerge in a completely transposed position, yet the aorta receives aerated blood This is achieved by inversion of the atria, or the atria and ventricles, or the ventriculobulbar loop There may be an associated ventricular septal defect

PATHOGENESIS OF THE COMPLEX Should there be no other associated anomalies, the heart may function normally Because of abnormalities in the AV node and bundle, there may be AV block.

TRICUSPID ATRESIA AND STENOSIS COMPLEXES

In these complexes, the tricuspid orifice is either absent or smaller than usual Always associated with these are (1) a diminutive right ventricle, (2) an atrial septal defect, and (3) left and right atrial and left ventricular hypertrophy.

Tricuspid Atresia or Stenosis without Transposition. In the complexes without transposition of the arterial trunks (Edwards and Burchell; Gasul et al.; Lev, 1953), there are three basic types (Fig. 6-8A, B). (1) There is a ventricular septal defect of varying size. If the defect is small, there is a small but functioning right ventricle with a small pulmonary artery. If large, then the pulmonary artery may be normal in size or even larger than the aorta (2) There is either pulmonary or infundibular atresia and an absence of the ventricular septal defect and, hence, a nonfunctioning minute right ventricle. (3) There is tricuspid stenosis with pulmonary stenosis or atresia. Here the right ventricle is small in size, with a very thick wall and fibroelastosis of the endocardium. The ventricular septum is intact.

PATHOGENESIS OF THE COMPLEX The basic anomaly is the tricuspid atresia (see Chap 1). The foramen ovale remains open because of pressure in the right atrium. This opening is usually smaller than the tricuspid orifice, and hence there is a physiologic stenosis at the foramen ovale Thus the right atrium presents a pressure hypertrophy. The left atrium and left ventricle receive the combined pulmonary and right atrial flow and, hence, present a volume hypertrophy. If there is a ventricular septal defect, then the left ventricle contracts against decreased peripheral resistance and, hence, is less hypertrophied. The right ventricle is, in general, small because of decreased flow It may be normal in size, however, if there is a large ventricular septal defect If there is tricuspid stenosis and pulmonary stenosis or atresia, the pathogenesis of the thick right ventricular wall and of the fibroelastosis is obscure

Tricuspid Stenosis and Atresia with Transposition of the Arterial Trunks. In this group of complexes, there is complete transposition of the arterial trunks, which alters the morphology of the heart Depending upon the size of the ventricular septal defect, the aorta may be large or small Aortic or pulmonary atresia may occur.

Ebstein's Complex. In this complex (Gotzsche and Falholt; Brown et al.; Lev et al), the tricuspid valve is displaced downward into the right ventricle and divides this chamber into a thin-walled proximal and a thicker-walled distal segment (Fig 6-8C, D). The position of the tricuspid valve is often at the line of junction of the sinus and conus. The anterolateral leaflet is partly attached to the annulus, while the posterior is not at-

TABLE 11-2. ETIOLOGY OF BUNDLE BRANCH BLOCK

Type of BBB	*Type of patient*	*Cause of block*
Right	Young	Congenital heart disease Rheumatic heart disease Tricuspid lesions Chagas' disease
	Older	Arteriosclerotic heart disease Cor pulmonale: Acute Chronic
	Exceptional	Toxic factors Infections Tumors Gummas, etc.
Left	With coronary insufficiency	Arteriosclerotic heart disease with or without arterial hypertension Calcific aortic stenosis Syphilitic aortic insufficiency
	Exceptional	Tumors Gummas Chagas' disease Myocarditis, etc

in the study of congenital heart disease, having important implications from the standpoint of both electrogenesis and differential diagnosis

In older patients, the appearance of right bundle branch block is usually due to coronary arteriosclerosis. In such instances, the block is usually complete, with left axis deviation and counterclockwise rotation. Lead I usually exhibits a qRs configuration (with a slurred S wave), and lead III shows an rSr′ configuration.

Another common cause of right bundle branch block is *cor pulmonale*, in both its acute and chronic forms. Under these circumstances, ÂQRS is usually deviated to the right, with clockwise rotation and signs of right atrial enlargement, in addition to other classical signs of these conditions

Bundle branch blocks of any variety may appear in several forms of myocarditis, in thyrotoxicosis, in myocardial disease of unknown etiology, in myocardial tumors, cysts, gummas, trauma, etc. In addition, they may be caused by the *toxic effects* of several drugs, such as digitalis, quinidine, and Pronestyl, and also may appear in certain endogenous intoxications, such as hyperpotassemia due to acute or chronic renal insufficiency (Schlesinger and Benchimol, 1956).

CLINICAL FINDINGS

There are no symptoms that are diagnostic of bundle branch blocks, the clinical manifestations that may occur are due either to the etiologic factor involved or to an unrelated clinical syndrome.

There are, however, certain signs which may result from ventricular asynchronism and, therefore, are directly related to the bundle branch block. These signs are (King, 1928) a double cardiac impulse, a muffled and prolonged 1st sound, and a split 2d sound A presystolic gallop rhythm and a midsystolic apical murmur, if present, are not related to the block.

Under special circumstances, the physical signs may suggest the presence of bundle branch block. The most important clinical finding is a distinct and wide splitting of the 2d heart sound (Cossio et al., 1940).

Clinically, *left* bundle branch block may be suggested if there is a presystolic gallop rhythm without heart failure and *a split 2d heart sound with a late aortic component*, so that the reduplication is accentuated by expiration. In *right* bundle branch block, there is *a more distinct splitting of the 2d sound with a marked delay in the pulmonic component*, which is highly suggestive Left bundle branch block indicates in most patients a diffuse type of heart disease, whereas right bundle branch block is not necessarily a sign of serious cardiac involvement.

PROGNOSIS

Bundle branch blocks were formerly considered to have an ominous prognostic significance, it is now believed that it is not the conduction disturbance itself but the etiologic factor involved, especially the nature and degree of the myocardial damage, which dictates the prognosis in each case (Schreenivas et al)

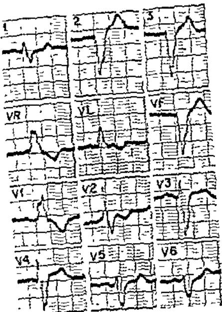
Although it is not rare to find bundle branch block as the sole manifestation of cardiac disease (in certain cases with a long survival), these conduction defects usually indicate an extensive myocardial damage, which in most patients is a result of arteriosclerotic heart disease.

The Wolff-Parkinson-White syndrome and other forms of preexcitation

EUGENE LEPESCHKIN

L. Wolff, J. Parkinson, and P. D. White described (1930) a syndrome which usually appeared in young persons with occasional paroxysmal tachycardia (but otherwise normal hearts) and was characterized by *a short P-R interval and a wide QRS complex* resembling bundle branch block. Many of these persons showed on other occasions normal QRS complexes with normal P-R intervals, the P-J interval to the S-T junction usually remaining the same length as in the aberrant complexes. Öhnell, who studied the syndrome extensively (1940), showed that it was caused by *premature excitation* of a part of the ventricle by the atrium, and introduced the term *preexcitation* to designate this as well as other less characteristic electrocardiographic patterns. In the typical pattern, the wide premature component of the QRS complex is of relatively low voltage and shows a distinct kink with the slender terminal portion of the QRS complex, which corresponds to normal activation of the ventricles through the AV node and is nearly identical in the normal and the aberrant complexes. In the vectorcardiogram, this premature portion usually moves two to three times more slowly than the rest of the QRS loop (Grishman and Jaffe, Wolff and Richman). The slow premature portion has been called by Segers et al (1947) *the delta wave*, as it resembles the Greek letter Δ in configuration (Figs. 11-39, 11-40).

In some cases, not only the initial, premature portion of the QRS complex but also its terminal portion is wide and slurred, and the form of the QRS complex is identical with that of bundle branch block. This pattern appears when normal activation through the AV node is delayed or absent, and the ventricles are activated exclusively in the premature manner, directly from the atrium. In such cases, the P-R interval of the normally conducted complexes is usually prolonged (Blum) or the AV bundle is completely interrupted (Mahaim, Scherf et al.). This pattern was designated as *type F* by Öhnell, but in order to avoid confusion with the grouping according to the direction of the delta wave, it will here be called *complete preexcitation*. In other cases, the premature component of the QRS complex is of very short duration and may be hard to distinguish from a normal slurred onset of the R wave, the duration of the QRS complex in these cases is accordingly not prolonged beyond the upper normal limits (Fig. 11-41). This pattern results when the normal conduction through the AV node is especially rapid, and only a small section of the ventricles can be excited directly from the atria before the rest of the ventricular mass is excited through the normal conducting system. It is usually seen in persons with normally short P-R intervals, such as children or young women. Relatives of persons with this pattern also tend to show a short P-R interval (Koch). This pattern has been designated as *type A* by Öhnell but will be called here *rudimentary preexcitation*, to avoid confusion. A third atypical pattern, designated as *type E* by Öhnell, shows the usual slurred configuration of the QRS complex but *a long or normal P-R interval*, and is due to a delay in both the normal and the premature excitation of the ventricle, the P-R interval of the normally conducted beats is always prolonged (Mahaim, Koch,





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masc. 34 years

Fig. 11-36(3). Complete right bundle branch with left axis deviation (−100°). The VCG in the horizontal plane shows a clockwise rotation of the QRS loop with its major portion oriented to the right and anteriorly. Note slight *counterclockwise rotation in the apical portion of the loop. Conduction delay is present in the afferent portion of the loop.* The VCG is diagnostic of right *bundle branch block and right ventricular hypertrophy.* Note that the initial portion of the efferent loop is directed leftward and slightly posteriorly, suggesting an associated left ventricular hypertrophy, particularly in the presence of marked left axis deviation.

TABLE 11-3 BUNDLE BRANCH BLOCK IN CONGENITAL HEART DISEASE

Type of BBB	*Cyanotic*	*Noncyanotic*
Right		
Ri [illegible]	[illegible]	[illegible] with severe pulmonary hypertension
Left axis deviation	AV communis	Ventricular septal defects with mild pulmonary hypertension Ventricular septal defects with or without atrial septal defects
Left	Tricuspid atresia	Coarctation of the aorta Aortic stenosis Patent ductus arteriosus (rarely)

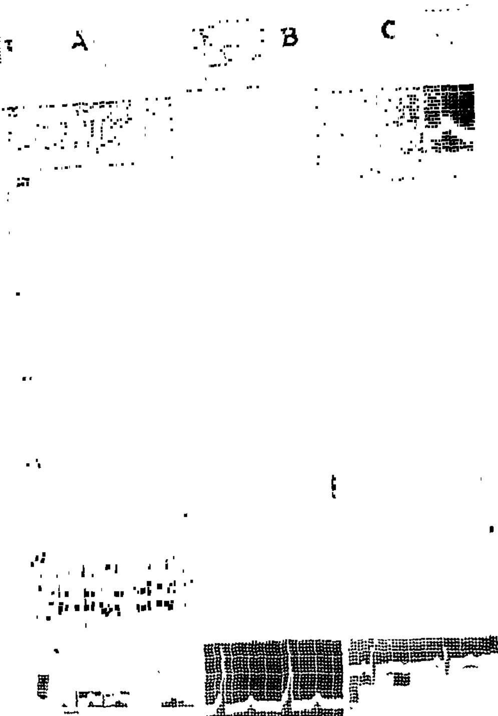


Fig 11-39 A Electrocardiogram of a 12-year-old girl *during* an attack of paroxysmal tachycardia *The P* waves follow the QRS complex and *are diphasic, but* mainly upright in leads I to III The QRS complexes are narrow, the *alternation* in amplitude of the R wave is *common* in *all* supraventricular tachycardias with *very high* ventricular rates. B. After termination of the attack, sinus rhythm with *type* B preexcitation is present. C After medication with quinidine, preexcitation *disappears The fusion of the T wave with the U wave is part of the* quinidine *effect.*

Right bundle branch block is usually considered to have a much less severe prognosis than left bundle branch block. Although this is true in most instances, one must consider each case from the clinical standpoint and not base the prognosis only on the type of bundle branch block.

Several investigators have attempted to determine the average survival time of patients with bundle branch block; some of them have found it to be relatively short. This would seem to indicate an unfavorable prognostic significance of these conduction disturbances. However, more recent statistical studies not only have shown much longer survival periods, but also have pointed out how difficult it would be to estimate how long patients can live with bundle branch block, because it is often impossible to determine the duration of the block prior to its recognition.

TREATMENT

There is no treatment of bundle branch block as such. Therapy must be directed toward the etiologic factors involved, when possible. Although there is no formal contraindication to the administration of *digitalis* in the presence of bundle branch block, if the conduction defect results from toxic effect of the drug, it is imperative to withdraw the medication, at least temporarily. *Quinidine* should be administered most carefully to these patients, under electrocardiographic control; administration should be stopped as soon as there is a further widening of the QRS complex or following the appearance of other types of conduction defect.

INTRAVENTRICULAR BLOCK

Under this designation, a series of intraventricular conduction disturbances has been described, in which the main branches of the bundle of His are not involved. The delay in activation occurs in the more distal segments of the conduction system or in restricted areas of the myocardium in the free ventricular walls. According to Segers, the absence of anatomic lesions of the branches of the bundle of His in certain cases exhibiting electrocardiographic changes which closely resemble those of bundle branch block suggests the possibility of a *focal block* with conduction delay in limited zones of the ventricular myocardium Because certain cases in which the EKG was characteristic of bundle branch block did not reveal, by electrokymographic studies, a delay in the onset of homolateral ventricular ejection, although a prolongation of the ejection period was observed, Segers suggests that the delay in the spread of the activation wave occurs in the lateral walls of the ventricle, representing what he has called *parietal block*. Other authors had previously described cases in which a conduction delay occurred in extensive areas of the ventricular walls at the distal ramifications of the conduction system Oppenheimer and Rothschild described cases with wide QRS complexes and low voltage under the designation of *arborization block*.

According to Grant, parietal block is due to disseminated lesions involving the anterior division of the left branch of the bundle of His; in these cases, the QRS complexes are not necessarily widened, the beginning of ventricular activation is normal, and the conduction delay occurs only in the lateral walls. This results in marked left axis deviation in view of the orientation of the terminal vectors, which are directed leftward and superiorly.

An electrocardiographic pattern showing deep S waves in leads II and III, exceeding the amplitude of the R waves, in the absence of S waves in lead I, has recently been described by Davies and Evans as due to a conduction disturbance in the peripheral branches of the left branch of the bundle of His. They attribute these lesions usually to ischemic changes and believe that the diagnosis of myocardial infarction is highly probable in patients with this type of EKG and with symptoms of cardiac pain.

When the focal lesion is more extensive and is localized in the subendocardial areas of the high anterolateral wall of the left ventricle, in addition to the involvement of the anterior division of the left branch of the bundle of His, resulting in left axis deviation, the initial portions of the QRS complex are also affected, and this has been called *peri-infarction block*, and is characterized by a wide Q wave which is associated with left axis deviation [Fig 11-36(4)].

The main electrocardiographic feature of the peri-infarction block is the widening of the angle between the initial and terminal 0.04 sec

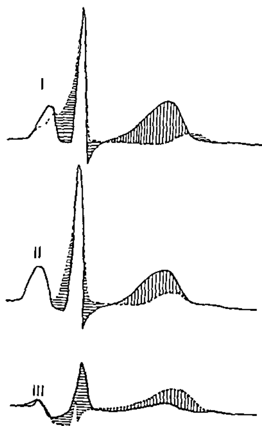


Fig. 11-40. The limb lead electrocardiograms of Fig. 11-39B are superimposed on corresponding leads of the same patient taken several weeks later when no preexcitation or quinidine effects were present. It can be seen that the increase in the positive area of the QRS complex (horizontal shading) is equal to the decrease in the positive area of the T wave and S-T segment (vertical shading).

Glushien and Goldblum, Pick and Katz). This pattern will be called *delayed* preexcitation.

According to the direction of the premature component of the QRS complex in the precordial leads, Rosenbaum, Hecht, Wilson, and Johnston distinguished two groups of cases. In "group B" this component is upright in the unipolar precordial leads V_3 through V_6 but inverted in V_1 (and sometimes also in V_2), the right, lower, and posterior portions of the thorax, and usually also aVF; in the frontal plane, this component shows usually left axis deviation but sometimes a normal axis In this group, the highest negative voltage of this component was found in leads from the right atrium near the tricuspid valve and in the lower esophagus, while leads from the cavity of the right ventricle and the coronary vein showed a positive premature component (Grishman et al., Giraud et al.; Hecht et al., 1957). This indicates that the prematurely excited ventricular muscle is *on the posterolateral epicardial surface of the right ventricle, near the AV groove.* In group A, the premature component of the QRS complex is negative on the back but positive in leads V_1 through V_6 and usually also in aVF, so that its axis in the frontal plane is usually normal or deviated to the right, and only occasionally deviated to the left. In intracardiac leads, some cases of this group showed the same findings as in group B, and the difference in the configuration of leads V_1 to V_2 in these cases was therefore attributed to a different position of the heart (Grishman et al.). However, in cases of this group

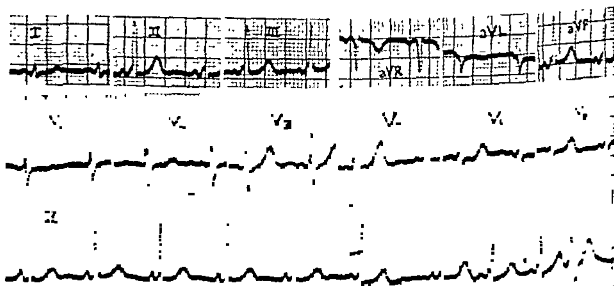


Fig. 11-41. Electrocardiogram of a 22-year-old woman with rudimentary preexcitation of type A, who complained of occasional rapid heart action. No electrocardiogram could be taken during the attack The lower strip shows "concertina effect," leading to pseudonormalization during the pressor phase of the Valsalva maneuver and to increased preexcitation during the postpressor phase. One ventricular extrasystole appears at the end of the tracing.

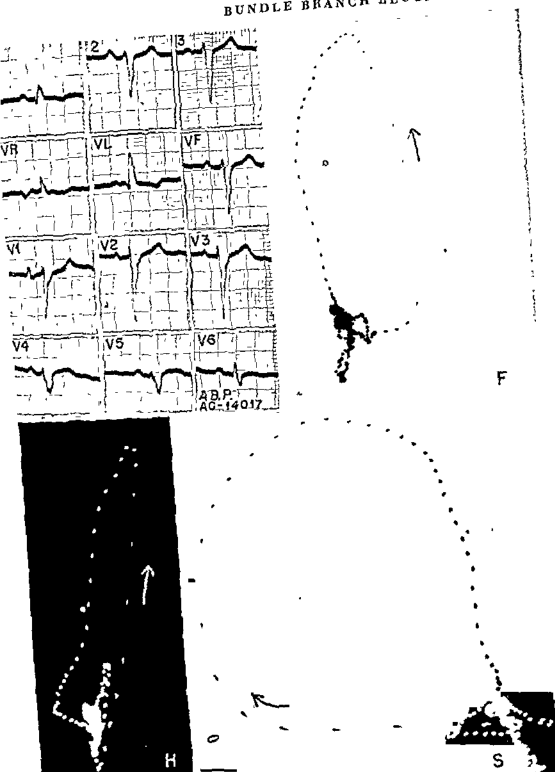


Fig 11-36(4). Focal peri-infarction block in a 67-year old male. The ECG displays wide Q waves in leads I and VL (high lateral infarction) associated with left axis deviation (- 85°) and a QRS duration of 0.12 sec. The VCG reveals a counterclockwise rotation in the horizontal plane, as well as a conduction delay in the terminal portions of the loop in the three planes

which showed an *isoelectric* or negative *premature component* in leads I and V_2, this component was positive in the right atrium and ventricle, but *deeply negative* in the coronary vein, which is in contact with the posterior aspect *of the left ventricle near the AV groove* (Giraud et al.). It was, therefore, concluded that *this is the site of the prematurely activated portion of the ventricle.* Such cases constitute *less than 20 per cent* of all persons with the Wolff-Parkinson-White syndrome. In both groups, the subepicardial location of the prematurely excited section accounts for the low voltage and long duration of the premature component of the QRS complex, since the rapidly conducting Purkinje fibers do not penetrate to the epicardium

Holzmann and Scherf and, independently, Wood and coworkers suggested that the premature excitation of the ventricle by the atria could take place through an *accessory* bundle similar to that first described by Kent (1893) This bundle consists of nonspecialized muscle and can, therefore, be expected to conduct excitation *more rapidly* than the specialized thin muscle fibers of the AV node, whose function is to delay excitation of the ventricle. A subepicardial accessory muscle bundle connecting the posterolateral aspects of the right ventricle and atrium was actually found in two cases with the preexcitation syndrome (Levine and Burge, Lev et al), and three similar subendocardial bundles were found in another case (Wood et al.), in still another case, the connection was between the atrial and ventricular septa on the right side (Segers et al , 1947) All these cases belonged to group B A subepicardial connection between the *left atrium and ventricle* was found in two cases (Öhnell, Mahaim), and an additional case showed both a *right-sided* and a *left-sided* connection (Kimball and Burch) All these cases belonged to group A and showed a negative premature component in lead I; the electrocardiographic pattern accordingly is in keeping with the anatomic location of the aberrant pathway On the other hand, the incidence of this pathway in routine autopsies is no greater than that of preexcitation (Lev *et al.*)

However, in several persons who had shown preexcitation, *no* accessory bundle could be found despite careful histologic study (Söderstrom, Hecht et al , 1957) In these cases, another explanation must be sought Holzmann and Scherf suggested that preexcitation can be due to stimulation of an acquired irritable ventricular center by the stretching effect of atrial contraction; such a center could also be set off by the action potential of atrial fibers (Segers et al , 1947) As these effects would be greatest *near the AV* border, especially if there is intimate contact between atrial and ventricular muscle fibers, as in the cases of Söderström and Langendorf et al., the localization of the premature component would be in keeping also with this hypothesis Stable preexcitation complexes were often seen to appear during cardiac catheterization, Giraud et al. found this in more than one-third of all catheterizations Prinzmetal et al (1952) could elicit such complexes most commonly by applying pressure, or a subthreshold electric current, to the inner surface of the ventricles through the atrium. In these cases, atrial contraction was probably transmitted mechanically through the catheter or the stimulating electrode. Preexcitation also could be elicited by injection of aconitine or epinephrine into the ventricular septum near the *AV* border (Frau and Maggi), and may also appear after intravenous injection of strophanthin (Vakil) or epinephrine (Fig 11-42) All these procedures increase ventricular excitability In all these cases, the complexes with short P-R interval and wide QRS complex usually showed transitions to ventricular parasystolic rhythms or coupled extrasystoles showing no relation to the P waves It is very difficult to decide in a *given* case whether true coupling of *the ventricular* complexes to the P *waves exists or* whether the relation between the wide QRS complex and the P wave is a fortuitous one Furthermore, there are many factors which may cause synchronization of P waves to the preceding QRS complexes (Rosenbaum and Lepeschkin), and the designation *of preexcitation* cannot be applied to *them True preexcitation* becomes probable *if the short P-R* interval remains *completely constant* during a series of beats *(Pick and Katz)*, but it can be proved definitely *only if this interval* remains constant even in the presence of spontaneous or *induced variations* of the P-wave rhythm A mechanical coupling can be expected to produce *a rather* loose synchronization, since the *instant* when a given tension is exerted on the *ventricle would* vary with the stroke volume,

of the QRS complex. With rare exceptions, in the presence of left axis deviation, when this angle exceeds 100° the EKG is diagnostic of anterolateral peri-infarction block. This type of conduction disturbance was initially described in 1950 by First and coworkers, who interpreted it as being due to the involvement of extensive areas of the subendocardial portions of the ventricles and of the Purkinje network. Under these circumstances, the impulse spreads through the noninvolved myocardium around the infarcted area, and its conduction is delayed at this point.

Finally, a type of *diffuse intraventricular block* has been described that resembles left bundle branch block, with Q waves in left precordial leads.

These cases are apparently due to a diffuse conduction disturbance through the ventricular wall, resulting from left ventricular hypertrophy, diffuse myocardial fibrosis, quinidine toxicity, or hyperpotassemia.

GRAPHIC DATA IN BUNDLE BRANCH BLOCK

PHONOCARDIOGRAM

The 1st sound is *prolonged* and lasts more than 0.16 sec. It is frequently of low amplitude. *Splitting of this sound* has been described by several authors. However, this observation is not confirmed by "stethoscopic" tracings and should be attributed to either inadequate or different techniques. Ventricular asynchronism results in the delay of the contraction of one ventricle over that of the other of about 0.04 to 0.05 sec. This interval is too short for causing a splitting of the central phase of the 1st sound, which lasts from 0.06 to 0.08 sec. However, it causes prolongation of the sound in both right and left bundle branch block. If *left* ventricular hypertrophy and intraventricular block add their effects to that of *left* bundle branch block, the delay between the contractions of the two ventricles may reach 0.06 sec or more. Then, closing of the mitral valve (first valvular event of the left heart) takes place at the time of opening of the pulmonic valve (second valvular event of the right heart) because the normal isometric tension period (about 0.05 sec) lasts as long as the pathologic interval between the contractions of the two ventricles. The phonocardiogram then reveals *three groups of vibrations.* the first is due to tricuspid closure; the second,

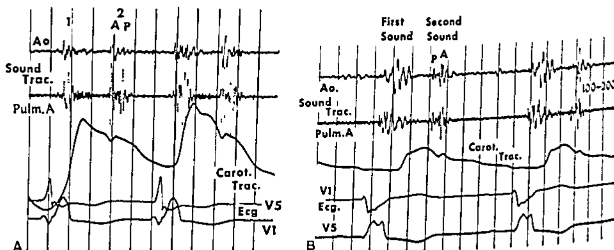


Fig. 11-37. A. Simultaneous phonocardiograms over the aortic (Ao) and pulmonic (Pulm. A.) areas, compared with carotid tracing and unipolar ECG chest leads. Time, 0.1 sec. The second component of the 2d sound is visible only in the pulmonic tracing and does not coincide with the incisura of the carotid pulse. Diagnosis: *right ventricular delay due to right bundle branch block.* M. Simultaneous phonocardiograms over the aortic (Ao) and pulmonic (Pulm. A.) areas, compared with carotid tracing and unipolar ECG chest leads. Time, 0.1 sec. The second component of the 2d sound is visible over both areas of the base and coincides with the incisura of the carotid pulse. The aortic 1st sound occurs later than the pulmonic 1st sound. Diagnosis: *left ventricular delay due to left bundle branch block.*

heart position, etc. An electrical coupling, on the other hand, would be much more constant, since the shape of the P waves and the sequence of activation of atrial muscle near the AV border show only insignificant variations.

A third hypothesis, advanced by Prinzmetal and coworkers (1952), is that the premature activation of the ventricle is due to accelerated conduction in part of the fibers of the AV node. Experiments considered as proof of this hypothesis are open to criticism (Sodi Pallares, 1956, Hecht et al., 1957). Furthermore, it would not explain the slow ascent of the premature component of the QRS complex, since premature activation of the rapidly conducting specific system would cause a rapid initial component

The incidence of the typical Wolff-Parkinson-White pattern is 0 02 to 0.04 per cent in children (Landtman; Vacheron), 0.07 to 0.1 per cent in apparently normal adults and in ambulatory patients (Hecht et al., 1957), and 0 16 per cent in hospitalized patients. This increased incidence with age and severity of disease, together with its appearance in infections or rheumatic heart disease, could be considered as favoring an acquired genesis of the syndrome The explanation of Pick and Katz, that any acquired factors which impair normal AV conduction would facilitate congenital aberrant conduction, does not seem plausible, since aberrant conduction takes place before normal conduction However, since conduction in aberrant anatomic pathways may be present only occasionally (Lyle), the increased incidence of aberrant complexes under abnormal conditions may be simply the result of the electrocardiograms being taken more often and in longer strips. On the other hand, the smaller incidence in children may be due to the short normal P-R interval, which may mask all or part of the aberrant conduction.

The fact that preexcitation was repeatedly found in two or more members of the same family (Öhnell; Koch; Hecht et al, 1957) is strongly in favor of a congenital origin of this anomaly, as are the occurrence of other congenital anomalies and the high incidence (0 7 per cent) of preexcitation in persons with congenital heart disease (Hecht et al, 1957) and the fact that preexcitation is twice as common in males as in females in all age groups (Vacheron; Lown et al.).

Increase of the heart rate, whether spontaneous or due to exercise, the Valsalva maneuver (Fig. 11-41), standing up, fever, atropine, amyl nitrite, or Banthine, usually causes the premature component of the QRS complex to become shorter and the QRS complex more normal, this is because of *acceleration of normal AV conduction*, which causes more of the ventricle to be activated in a normal manner. Occasionally, the premature component may disappear completely, this "pseudonormalization" can be distinguished from true normalization by the fact that the *P-R interval remains short* True normalization may occur also, in this case *the P-R interval becomes longer.* This can be explained by assuming either that

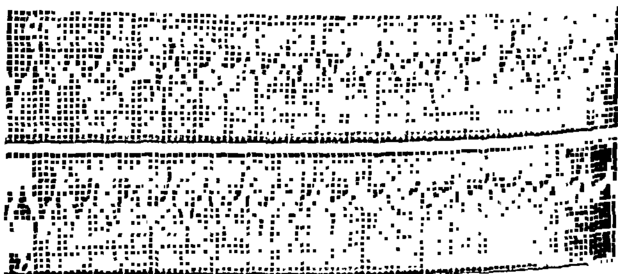


Fig. 11-42. Alternating preexcitation appearing in a cat after injection of myocardial sympathin. B The premature component of the QRS complex appears progressively later and disappears at the end of the tracing

to pulmonic opening plus mitral closure; the third, to aortic opening A similar phenomenon, with delay of right ventricular events, occurs when *right* intraventricular block and *right* ventricular hypertrophy add their effects to that of *right* bundle branch block.

It is probable that a new study by means of "selective phonocardiography," with its scanning of adjacent bands of sounds, will reveal different data, possibly including a "splitting" of the 1st sound. (The quotes are necessary because the 1st sound already presents a "physiologic" splitting when recorded in normal subjects in the band 240 to 480 cps)

The 2d sound, being shorter, is constantly split in bundle branch block In the case of *right bundle branch block*, as the pulmonic component normally follows the aortic component of the 2d sound by 0 02 sec, the 2d sound is widely split, and there is an interval of about 0 05 to 0 07 sec between the aortic and the subsequent pulmonic component (Fig 11-37A) In the case of *left bundle branch block*, the opposite occurs If there is only a slight delay of the aortic component, it will fall at the time of the pulmonic component (*no splitting of the 2d sound*) If, on the other hand, there is a severe delay, then the aortic component will follow the pulmonic component by 0 02 to 0 04 (*paradoxical splitting of the 2d sound*, Leatham) (Fig 11-37B)

CAROTID TRACING, JUGULAR TRACING

The delay between the beginning of the 1st sound and the rise of the carotid pulse (usually about 0 05 sec) is *increased* and lasts from 0 07 to 0 08 sec in *left bundle branch block*. The incisura of the carotid pulse coincides in normal subjects with the main vibration of the 2d sound (aortic component) In *left bundle branch block*, it coincides with *the 2d phase* of the split 2d sound (aortic component) (Fig 11-37B) The rise of the carotid pulse has a normal relationship to the beginning of the 1st sound in *right bundle branch blocks* The incisura has a normal relationship to the 1st phase of the split 2d sound (aortic component) in this type of block (Fig. 11-37A) while the pulmonic component occurs later

In *right bundle branch block*, the study of the jugular tracing is of importance. *the peak of the V wave is markedly delayed* and occurs 0 08 to 0.14 sec after the end of the 2d sound (or after the 2d phase of the 2d sound, if this is split). In other words, the V wave, which usually occurs 0.08 to 0.14 sec after the 2d sound, has the same relationship to the pulmonic component (2d phase) of this sound, when it is split.

ELECTROKYMOGRAM

This method may be applied to the study of pulmonic or aortic pulsations. In most cases, it may be applied to the study not only of left ventricular but also of right ventricular contraction. Moreover, right atrial tracing is so deeply influenced by right ventricular contraction that the phases of right ventricular dynamics may be studied even by recording a right atrial border tracing The best technique is that of recording simultaneously a high left ventricular tracing and a pulmonic tracing, then, a right ventricular (or right atrial) tracing with an aortic tracing[2] The study may be completed by the simultaneous observation of the anterior (right ventricle) and posterior (left ventricle) surfaces of the heart It should be kept in mind that while direct comparison of the two ventricles has a decisive importance, comparison of one ventricle with one pulse (or of the aortic and pulmonic pulses) is less significant on account of possible interaction of peripheral factors which may accelerate or delay the valvular events.

Normal time relationships between the two ventricles and the two large vessels were studied by the author and his coworkers (1948) and by Samet and coworkers (1950b) In spite of slight individual and phasic variations, it can be assumed that the two ventricles and the two large arteries present pulsations which succeed each other within 0 02 sec. The most common is the precession of the pulmonic pulse by 0.020 sec (Part 4, Chap. 8).

In about 30 per cent of the cases of *left bundle branch block*, left ventricular contraction and the aortic pulse are delayed over the

[2] If one has only a pickup unit, the study should be made in the following way· (1) aortic electrokymogram (EKy) plus sound tracings, (2) pulmonic EKy plus sound tracings, (3) left ventricular EKy plus sound tracings, (4) right ventricular (or right atrial) EKy plus carotid and sound tracings, (5) comparison of the four tracings using the sound tracing as timer It should be noted that use of the carotid tracing as timer is confusing in these cases of bundle branch block because the carotid pulse is necessarily delayed in left bundle branch block.

at high heart rates conduction in an anatomic aberrant pathway does not take place because of fatigue, or that the mechanical effect of atrial contraction is smaller because of the decreased stroke volume On the other hand, decrease of heart rate, such as that caused by carotid sinus pressure, the late phase of the Valsalva maneuver (Fig 11-41), or medication with *Prostigmine*, *Mecholyl*, or digitalis, usually increases the duration and magnitude of the premature component of the QRS complex because of slowing of normal AV conduction During this effect, the P-R interval remains short but the P-J interval increases In many cases, the above factors led to the appearance of preexcitation complexes

The remarkable constancy of the P-R interval in preexcitation may be due to the fact that an aberrant pathway, consisting of nondifferentiated ventricular muscle, would not be influenced by the vagal effects which cause prolongation of the normal AV conduction together with bradycardia It would also be in keeping with an electrical, but not with a mechanical, excitation of a ventricular irritable focus by the atrium, as mentioned above The only factors which influence the P-R interval seem to be *quinidine* and *procaine amide*, which usually cause the premature component of the QRS complex to appear progressively later, to become smaller, and finally to disappear completely (Blinder et al , Zapata Dias et al) In these cases, the P-R interval becomes longer while the P-J interval is usually unchanged In some cases, normalization takes place abruptly The action of these drugs would be in keeping with a slowing of conduction in an accessory bundle, but not in the AV node, since they have a greater effect on nonspecific ventricular muscle It would also be in keeping with an ectopic ventricular focus stimulated by atrial activity, as the same drugs decrease ventricular excitability, a gradual and considerable prolongation of the P-R interval would be more difficult to explain on this basis, since the moment of excitation would then occur considerably after the maximal electrical and mechanical effects of atrial excitation The occurrence of delayed preexcitation would also be difficult to explain on this basis Finally, the occurrence in some cases of preexcitation of Wenckebach's periods, i e , of progressive prolongation of the P-R interval leading to complete AV block followed by shortening of the P-R interval (Levine and Burge, Scherf et al., 1953; Hecht et al., 1957), could not be explained on any other basis except that of an aberrant AV bundle.

When AV nodal beats occur in preexcitation, either spontaneously or during the initial, bradycardiac action of atropine, during carotid sinus pressure, or after injection of Neo-synephrine (Ohnell), they always show a normal QRS complex if the P wave follows the QRS complex. In these cases, the ventricle is excited entirely through normal pathways before preexcitation can take place Occasionally, when the P wave precedes the QRS complex slightly, a delta wave may appear, but it is always shorter than in the usual preexcitation complexes In a few cases, this wave was present even when no P wave preceded the QRS complex; in these cases the rhythm could have originated in the accessory bundle, or this bundle could have originated in the AV node itself

Paroxysmal tachycardia was found in about 70 per cent of all cases showing the Wolff-Parkinson-White pattern, in children, this percentage was 93 per cent (Vacheron). On the other hand, it constitutes about 5 per cent of the cases of paroxysmal tachycardia, in children this percentage was 12 per cent (Nadas et al) The higher incidence in children can be explained by the fact that electrocardiograms in children are seldom taken unless there is a conspicuous alteration of rate or an arrhythmia In most cases the QRS complexes were regular and narrow, and were followed after about 0.10 sec by inverted or diphasic P waves, the premature portion of the QRS complex was absent. The tachycardia was therefore designated as nodal, but, in contrast to typical nodal tachycardia, the P waves were often upright in lead I The appearance of this type of tachycardia can be explained by means of a special form of "circus movement" from the ventricle to the atrium through an accessory AV bundle, and back to the ventricle through the normal AV conduction system. It could not be explained at all on the basis of an excitable ventricular center, for this would cause a ventricular tachycardia.

The beginning and end of the paroxysmal tachycardia was studied repeatedly only in a few cases. In two of them (Juncadella Ferrer.

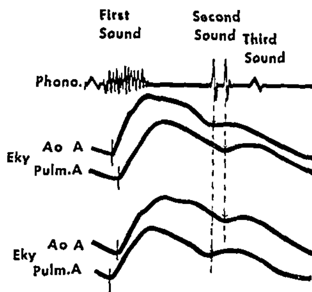


Fig. 11-38. Scheme of the electrokymograms of the aortic and pulmonary arches in right (above) and left (below) bundle branch blocks with ventricular asynchronism. (*From Luisada. Heart Beat Hoeber, 1953.*)

right ventricular and the pulmonic pulse by about 0.03 to 0.05 sec (Fig 11-38). If there is hypertrophy or intraventricular block of the left side, the delay is greater. Hypertension of the greater circulation increases the delay revealed by the rise of the pulse, decreases that revealed by the incisura.

In about 30 per cent of the cases of *right bundle branch block*, the right ventricular contraction and the pulmonic pulse are delayed over the left ventricular and the aortic pulse by about 0.03 to 0 05 sec (Fig. 11-38). If there is hypertrophy of the right ventricle or intraventricular block of the right side, the delay is greater. Hypertension of the lesser circulation increases the delay revealed by the rise of the pulse, decreases that revealed by the incisura. Systemic hypertension may partly neutralize the effect of right bundle branch block, so that the delay is less apparent.

In both types of block, a prolongation of the phase of isometric relaxation was observed A large percentage of cases of bundle branch block, whatever the side, seem to present a bilateral delay of contraction upon EKy studies Phonocardiographic studies reveal a much larger percentage of asynchronism than EKy studies.

Tommaselli), frequent atrial extrasystoles were present; if they appeared late, they were followed by QRS complexes with delta waves, but if they appeared early enough, they were followed by a narrow QRS complex, followed in turn by a diphasic P wave and an access of paroxysmal tachycardia. Still earlier extrasystoles were followed by narrow QRS complexes only, or were blocked. Apparently circus movement becomes possible only if an atrial extrasystole appears early enough to find the accessory bundle still refractory but late enough for it to recover by the time excitation is conducted to the ventricle The attack was terminated either by a diphasic P wave after progressive lengthening of the P-R interval (block in the AV node) or suddenly by a QRS complex (block in the accessory bundle). In other cases (Rosenbaum et al., 1945; Katz and Pick), the attacks were initiated in the same way by lower nodal extrasystoles, with the first few complexes of the tachycardia showing a wide QRS complex without a slow initial component, because of aberrant intraventricular conduction. In the case of Lyle, the atrial extrasystoles elicited runs of tachycardia with wide QRS complexes showing delta waves, in this case, the normal conducting system could have been still refractory while excitation was conducted down the accessory bundle, but became conducting by the time excitation reached it retrogradely from the ventricle These cases show that a premature stimulus is necessary to establish circus movement and explain the numerous observations in which no paroxysmal tachycardia appeared until the occurrence of some acute infection, which could have precipitated extrasystoles responsible for circus movement In most cases the tachycardia can be interrupted by digitalis, while in some, quinidine is more effective This can be explained by assuming that circus movement can be terminated either by blocking the AV node with digitalis or by blocking the accessory bundle with quinidine

In a minority of the cases with preexcitation, *atrial fibrillation* is registered during the accesses of paroxysmal tachycardia, and a few cases show *atrial flutter* (Pick and Katz). The case of Tommaselli shows clearly how the typical "nodal" type of tachycardia attributed to circus movement through the aberrant bundle can be transformed into atrial flutter and finally into atrial fibrillation; any rapid stimulation of the atria can lead to the same sequence. These arrhythmias can accordingly be explained on the basis of an accessory bundle, but not on that of an excitable ventricular center. When atrial fibrillation is present, runs of normal QRS complexes usually alternate with groups of complexes showing very wide delta waves (complete preexcitation). These groups can be explained by assuming that when excitation takes place over the accessory bundle, the normal AV bundle is excited later and retrogradely, and therefore recovers its conductivity later than the accessory bundle, so that the constantly circulating fibrillation waves are likely to enter the accessory bundle again (Pick and Katz). As in atrial fibrillation, coordinated atrial contractions are absent, the appearance of preexcitation in these cases cannot be explained by mechanical effects of atrial contraction, while stimulation by electrical effects would still be possible. One peculiarity of atrial fibrillation with preexcitation is that the ventricular rate is usually very rapid, and the usual slowing effect of *digitalis* medication on this rate is absent (Katz and Pick, Giraud et al.). This can be explained by the fact that this slowing effect is due to a blocking effect of digitalis on the AV node, the drug would not have effect on a muscular accessory pathway. *Quinidine*, which blocks also the accessory pathway, must be combined with digitalis in such cases.

In many cases of preexcitation, the paroxysmal tachycardia was interpreted as being of ventricular origin, but closer scrutiny of the tracings always made it seem probable that in reality *atrial fibrillation with complete preexcitation* was present (Langendorf et al; Giraud et al.) True ventricular tachycardia becomes probable only in cases where ventricular extrasystoles of the same form had appeared previously (Frau and Maggi). In these cases, the explanation of the syndrome as due to an excitable ventricular center is more likely.

Occasionally the slope of the premature component of the QRS complex in preexcitation complexes may be so slight that this component can be mistaken for an ascending P-R segment; if this slope is less than 2.5 mv/sec, the term "type B" was used by Öhnell, but we shall call this pattern *low-voltage preexcitation*. This type often results from superposition of a descending P-R segment

on the delta wave and usually becomes more typical with slowing of the heart rate, especially in the precordial leads. A much more common pattern shows a short P-R interval but an apparently normal QRS complex. It can represent preexcitation with a very steep and rapid delta wave, but this diagnosis can be made with certainty only if QRS complexes of different configuration and with a longer P-R interval can be observed to appear. In this type of "rapid preexcitation," designated as "type C" by Ohnell, the accessory bundle could terminate in the bundle of His. On the other hand, the pattern can correspond to accelerated conduction in the AV node. Lown et al found that the incidence of paroxysmal tachycardia in such cases was much less than in typical preexcitation (only 10 per cent), while the percentage of cases among females was much greater (70 per cent), most of them had signs of adrenal cortical overactivity. In some of these cases, the P-R interval became longer after digitalis administration but the QRS complex remained identical, and in these an accessory bundle could be definitely excluded.

The recognition of preexcitation is important, first of all because, although deaths due to paroxysmal tachycardia have been reported in this condition, its prognosis is much better than that of left bundle branch block with which it may be confused. The differentiation is easy in the presence of a typical delta wave, but complete preexcitation may look almost exactly like bundle branch block, especially if the P-R interval is borderline or atrial fibrillation is present. Usually, the initial slope of the QRS complex in right precordial leads is steeper in bundle branch block than in preexcitation, but sometimes a definite diagnosis can be made only by conversion to sinus rhythm or by application of agents which cause acceleration of AV conduction or true normalization. A Valsalva maneuver or subcutaneous injection of 1 mg atropine may cause the appearance of nodal escape beats with a normal QRS complex, accelerated AV conduction, or pseudo normalization. Slow intravenous injection of procaine amide at the rate of 200 mg/min up to 1 Gm caused normalization in 7 out of 9 cases without side effects (Zapata Dias et al.).

Preexcitation complexes showing a negative delta wave in leads I or II or III may imitate the deep Q wave of myocardial infarction. On the other hand, positive delta waves may prevent the deep Q waves of infarction from appearing, and old infarction can be recognized in such cases only after normalization. The changes of the R wave and S-T segment caused by infarction can also be masked by preexcitation, but in most cases, closer inspection allows their recognition. The secondary changes of the T wave and S-T segment in [illegible]tation are always opposite in direction [illegible]

[illegible] ponent (Fig 11-40). The total QRS [illegible] (ventricular gradient) remains the same (Bercun et al.). Accordingly, if the S-T segment [illegible] elevated in a lead where the premature [illegible]

[illegible] tive or only slightly positive, these changes [illegible] ease to be primary and to indicate additional myocardial damage. It must be emphasized, however, that the primary T-wave inversion may appear in preexcitation without myocardial infarction after accesses of paroxysmal tachycardia, especially if treated with quinidine, in these cases, the T-wave changes remain after normalization. Another source of error may appear in rudimentary preexcitation, where the change in the QRS area may not be sufficient to cause an abnormal configuration of the QRS complex but sufficient to cause depression of the S-T segment and a diphasic T wave, which can be erroneously interpreted as denoting myocardial damage.

In the presence of paroxysmal tachycardia, the recognition of preexcitation is important for treatment, since if circus movement through the accessory bundle is the cause of tachycardia, quinidine or procaine amide should be beneficial even if this appears to be "supraventricular." Quinidine will also prevent the appearance of single atrial extrasystoles, which are often instrumental in precipitating an attack. Recently Chlorpromazine has been found beneficial, alone or in conjunction with procaine amide, even where the latter alone was ineffectual (Giraud et al.). The presence of upright P waves in lead I in "nodal tachycardia" or of the peculiar groups of wide QRS complexes in atrial fibrillation makes preexcitation probable, but it can be established only when delta waves can be identified in previous tracings or appear between attacks. It must be emphasized that after the tachycardia has

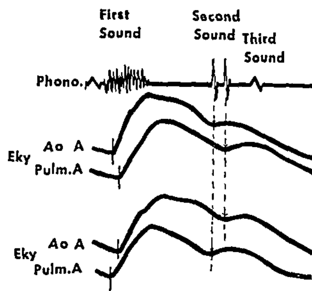


Fig. 11-38. Scheme of the electrokymograms of the aortic and pulmonary arches in right (above) and left (below) bundle branch blocks with ventricular asynchronism. *(From Luisada. Heart Beat. Hoeber, 1953.)*

right ventricular and the pulmonic pulse by about 0 03 to 0.05 sec (Fig. 11-38). If there is hypertrophy or intraventricular block of the left side, the delay is greater. Hypertension of the greater circulation increases the delay revealed by the rise of the pulse, decreases that revealed by the incisura.

In about 30 per cent of the cases of *right bundle branch block,* the right ventricular contraction and the pulmonic pulse are delayed over the left ventricular and the aortic pulse by about 0.03 to 0.05 sec (Fig. 11-38) If there is hypertrophy of the right ventricle or intraventricular block of the right side, the delay is greater. Hypertension of the lesser circulation increases the delay revealed by the rise of the pulse, decreases that revealed by the incisura. Systemic hypertension may partly neutralize the effect of right bundle branch block, so that the delay is less apparent

In both types of block, a prolongation of the phase of isometric relaxation was observed. A large percentage of cases of bundle branch block, whatever the side, seem to present a bilateral delay of contraction upon EKy studies Phonocardiographic studies reveal a much larger percentage of asynchronism than EKy studies.

been stopped with quinidine, preexcitation complexes may not appear as long as the quinidine effect persists; an electrocardiogram repeated several days after termination of treatment is therefore more likely to disclose preexcitation (Blinder et al.). The ultimate goal in the treatment of tachycardia due to preexcitation would be to remove surgically the accessory bundle or the point of intimate contact between atrial and ventricular muscle. Its precise localization can be made satisfactorily from the configuration of the delta wave.

11

Double rhythms (pararrhythmias)

CORNELIO PAPP

One of the basic laws of cardiac physiology is that "a pacemaker working at a faster rate suppresses any potential secondary *or tertiary* pacemaker having a lower rate." Since, under normal conditions, the SA node forms impulses at a faster rate than the AV node *or the intraventricular* centers, in normal conditions it remains in sole control of cardiac *rhythm*.

In *double rhythms*, two pacemakers are active simultaneously, one of which is usually the SA node The secondary *pacemaker*, which may be situated anywhere in the atria, the node, the bundle, or its *branches*, may form *impulses* at a higher or lower rate than the SA node For the existence of a double rhythm, it is essential that the slower *pacemaker be* protected from the faster one Such a "protection block" has been shown to exist *and* prevents the suppression of the rhythm created by the SA node or the *ectopic* pacemaker, whichever is the slower of *the two*

Double rhythm may manifest itself in two different forms

1 *AV dissociation* Here the rhythm of the atria is directed by the SA node, that of the ventricles, by the AV node. The SA rhythm, usually slower, is protected by a unidirectional block which prevents the nodal impulse from spreading backwards to the SA node, while there is no obstacle to the spreading of sinus impulses to the AV node The conducted SA impulses produce a transient disturbance of the AV nodal rhythm (dissociation with interference)

2 *Parasystole* The SA node is in command of atria and ventricles An ectopic (usually ventricular) pacemaker working at a slower rate, is protected by a *block of entry* from the *faster* SA impulses. This block, too, is unidirectional and allows the ectopic pacemaker to assert itself and to interfere *with the basic* rhythm.

The main difference between these two double rhythms—apart from the dissociated activity of the two pairs of chambers in AV dissociation—consists in the way the two pacemakers interfere with each other. In AV dissociation, it is the SA node which disturbs the ectopic pacemaker, while in parasystole, it is the ectopic pacemaker which interferes with the SA rhythm.

ATRIOVENTRICULAR DISSOCIATION

When the rate at which impulses form in the AV node is superior to the rate at which it receives impulses from the SA node, AV *nodal rhythm* results. This *condition arises* when impulse formation is depressed in the SA node or exalted in the AV node, or when both these conditions exist. Since the physiologic property of the nodal tissue is that of unidirectional conduction, and impulses are transmitted readily from atrium to ventricle (but only with difficulty in the reverse direction), *retrograde block* may arise and the SA node will continue to beat independently. How many of the SA impulses are so timed as to fall outside the refractory period and "capture" the ventricle depends upon the relative rates of the two pacemakers and the duration of the refractory period of both the junctional tissues and the ventricles. If the AV nodal rhythm is rapid, the refractory period shortens, and, with a slow SA rhythm, ventricular

tached at all. The septal leaflet may or may not be attached. The new "tricuspid orifice" may be small or large and may be normal functionally or the seat of an insufficiency or, less commonly, stenosis There is usually a patent foramen ovale The right atrium is hypertrophied and dilated. The proximal part of the right ventricle is dilated. The distal part of the right ventricle may be hypertrophied or normal in thickness The left atrium and ventricle may be normal or hypertrophied The pulmonary artery is usually small Fibroelastosis is often present in the proximal right ventricular chamber. The conduction system may be normal, or accessory muscle bundles may bridge the right atrium and ventricle

PATHOGENESIS OF THE COMPLEX. The displaced tricuspid orifice may be considered to be the basic anomaly. Thus, the right atrium and proximal part of the right ventricle act as a unit, although the exact method of their functioning is not clear. There is usually decreased pulmonary flow. If there is a functional tricuspid stenosis, then there is a venoarterial shunt at the atrial level, and hence the left atrium and ventricle may present a volume hypertrophy, if not counterbalanced by the decreased pulmonary flow.

Hypoplasia of the Aortic Tract Complexes. In this group (Lev, 1953) the following common denominators exist (Fig 6-9A): (1) The aortic orifice, the ascending and the trans-



Fig. 6-8 ... atresia B ... cuspid atr... ed, R, diminutive right ventricle. ...inutive right ventricle. T, tricuspid ... right atrial and proximal right ventricular chamber D View of tricuspid valve and conus RA, right atrium, Pr, proximal chamber, C, conus (C D. From M. Lev Autopsy Diagnosis of Congenitally Malformed Hearts. Charles C Thomas, 1953)
C. Ebstein's disease. View of

verse portions of the aorta are small. (2) The pulmonary artery and its orifice are large. (3) The left side of the heart is hypoplastic. (4) The right side of the heart is markedly enlarged. (5) There is a widely patent ductus. (6) There is an atrial septal defect (7) There is no transposition of the arterial trunks. In the simplest form, the above are the findings with a functioning left ventricle and no fibroelastosis. In another form, there is aortic stenosis or atresia with a small, but functioning, mitral orifice Here the left ventricle is small, with fibroelastosis In still another form, there is combined aortic and mitral atresia with a minute nonfunctioning left ventricle

PATHOGENESIS OF THE COMPLEX The embryogenesis of this complex is discussed in Chap. 1. After birth, there is increased pulmonary flow and hence left atrial flow This is shunted through the atrial septal defect, producing a volume hypertrophy superimposed on the pressure hypertrophy of the right ventricle, produced by the "reversed" ductus. Where there is mitral and aortic atresia, this process is greatly exaggerated.

Coarctation of the Aorta Complexes. In coarctation of the aorta (Mustard et al., 1955, Reifenstein et al.), there is a narrowing in some part of the aorta, usually the isthmus, although the narrowing may be present in the thoracic or the descending aorta Where it is present in the isthmus, there are two types of complexes associated with this abnormality —the adult (postductal) and the fetal (preductal) types.

ADULT TYPE. In the adult type of complex, the narrowing is usually just distal to the point of entry of the ductus or *ligamentum arteriosum*, but it may be present just at, or proximal to, the ductus (Fig. 6-9B). Uncommonly, an adult form may have the constriction beginning at the innominate or left subclavian and becoming gradually more severe at the approach of the ductus, or the initial constriction may be followed by dilatation and then constriction again Occasionally, eventually, there may be complete atresia of part of the transverse arch. In this form of complex, the left ventricle is hypertrophied and there is dilatation of the ascending aorta In about 10 per cent of the cases, there is a *patent ductus arteriosus*, usually of small caliber. There may be an associated *aneurysm of an aortic sinus of Valsalva* and a *bicuspid aortic valve* and, occasionally, a *left superior vena cava* After 12 years of age, the intercostal arteries become enlarged and tortuous. The aortic ring may become dilated, with resultant aortic insufficiency Likewise, the aorta distal to the constriction is often dilated.

PATHOGENESIS OF THE COMPLEX. There is *hypertension* proximal to the coarctation, with



Fig 6-9. A. Hypoplasia of the aortic tract complex. Anterior view. A, aorta; P, pulmonary artery. B. Adult coarctation in a child. Arrow points to the coarctation. (From M. Lev. Autopsy Diagnosis of Congenitally Malformed Hearts. Charles C Thomas, 1953)

been stopped with quinidine, preexcitation complexes may not appear as long as the quinidine effect persists; an electrocardiogram repeated several days after termination of treatment is therefore more likely to disclose preexcitation (Blinder et al.). The ultimate goal in the treatment of tachycardia due to preexcitation would be to remove surgically the accessory bundle or the point of intimate contact between atrial and ventricular muscle. Its *precise localization* can be made satisfactorily from the configuration of the delta wave.

to drugs, and 8 with unexpected standstill, usually occurring during surgery (Zoll, et al., 1956a).

The first condition to be considered, Stokes-Adams attacks, occurs in patients with AV block and consists of attacks of cerebral ischemia due to very slow idioventricular rates, ventricular standstill, ventricular tachycardia, or ventricular fibrillation (Parkinson et al., 1941). The attacks are manifested by dizziness, syncope, prolonged unconsciousness, and convulsions, and they may end in death. The cardiac origin of such seizures becomes clear when cardiac arrest is observed during an attack, by the absence of a pulse or heart sounds. A more exact diagnosis is usually

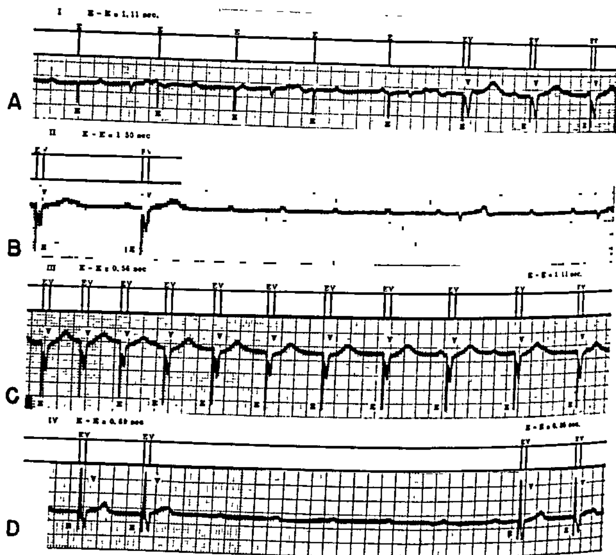


Fig 11-47. External electric stimulation in a patient with Stokes-Adams attacks. Lead aVF; standardization half-normal (1 mv equals 5 mm) A Interruption of idioventricular rhythm by faster externally paced beats The intensity of the electric stimuli, *E*, was progressively increased until ventricular responses, *V*, were produced. Three spontaneous idioventricular complexes (cycle length, 2 04 sec) occurred during ineffective stimulation; during effective stimulation at a faster rate (cycle length, 1 11 sec) they were suppressed. B. Resumption of idioventricular rhythm following external stimulation. When stimulation was stopped, the spontaneous ventricular pacemaker reappeared after a pause of 4.64 sec and regained its previous rate within three beats. C. Effective stimulation at varying rates. Each stimulus, *E*, produced a ventricular response, *V*. Each electrocardiographic ventricular response depended upon an electric stimulus, as shown by the constant relationship at widely varying rates of stimulation. D. Ventricular standstill during temporary interruption of stimulation. During a test period of 5.5 sec no stimuli were applied. No spontaneous ventricular contractions occurred during this interval, and the patient lost consciousness. Resumption of stimuli immediately gave ventricular responses, and the patient revived at once. (*Reprinted by permission of Grune & Stratton, from Circulation, 1954.*)

Since in most of the published cases, the ventricular rate was faster than the atrial rate, this was thought to be an essential feature of AV dissociation Laubry and Lequime (1933) and Laubry and Poddu (1936) proved that this is not necessarily so and that certain factors (digitalis, toxic agents), which may produce SA depression and a passive escape of the node, may also exalt nodal activity They published cases with ventricular rates faster than or similar to the SA rates (*isorhythmic dissociation*).

The QRS complexes are commonly supraventricular. They may have a bizarre shape, because of aberrant intraventricular conduction caused by early appearance (Fig. 11-44B) of an infranodal pacemaker.

The QRS complexes conducted from the SA node may have a slightly different shape (Fig

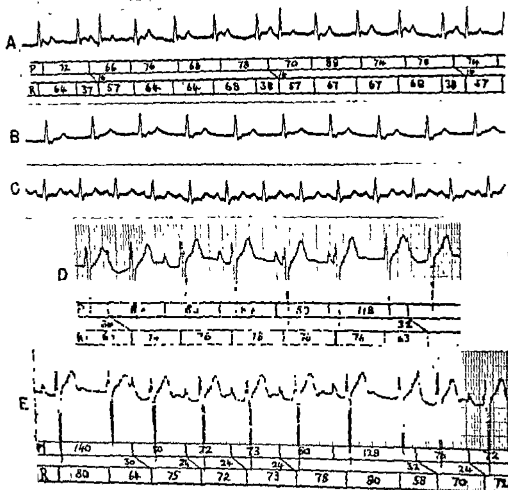


Fig. 11-43 Lead II A. *Mar. 27, 1957* AV dissociation with *interference;* third, eighth, and last beats, which are premature, are conducted. B. *Mar. 29* nodal rhythm with *retrograde* conduction. C *Apr 1*· regular sinus rhythm Man aged 21, *surgical* repair of atrial septal defect under hypothermia, Mar 26, atrial flutter *during operation*, 1 mg *digoxin* (Lanoxin) injected, no further digitalization D AV dissociation with interference *secondary* to sinus *arrhythmia* and bradycardia, *latent* heart block Bipolar right atrial lead *from* second right intercostal space and fourth left intercostal space on sternal border *with* double amplification shows upright P waves throughout Subject is at rest, first and last P waves following AV nodal *beats are* conducted, other beats are dissociated E After exercise; sinus is in *command* for four successive beats, P-R *interval* of conducted beats in late diastole *shortens* from 0.34 to 0.24 sec. Man aged 21, atrial septal defect and *syncopal* attacks; the latter subsided *after* AV *nodal automatism* became established.

made by the observation of a very slow heart rate due to an idioventricular rhythm between attacks, however, *it is important to remember that evidence of any degree of AV block between attacks establishes the diagnosis* and that, at times, in a patient with this disease, *the pulse rate may be normal* and AV conduction *may be normal*, with a P-R interval of less than 0 20 sec

There are three major problems in the *treatment of Stokes-Adams attacks: (1) emergency resuscitation from a major attack*, (2) termination of persistent ventricular standstill, and (3) prevention of frequently recurrent attacks.

For a major attack with persistent syncope, emergency resuscitation must be effected promptly and the circulation to the heart and *brain must be restored within 3 or 4 min* Electrocardiographic identification of the mechanism of the attack is useful but, even when an electrocardiogram is not available, *treatment must be immediately instituted*

If the mechanism of the attack is ventricular standstill or is unknown, *the precordium should be struck forcefully* Then *cardiac puncture* should be performed, the tip of the needle should be embedded in the heart wall, and the hub of the needle should be tapped sideways *repeatedly to stimulate* ventricular beats If arrest persists, *epinephrine hydrochloride* may be injected through the needle into a cardiac chamber, care being taken not to put any within the myocardium

These measures should be tried in sequence if there is delay in applying the electric pacemaker They are *simple* and usually immediately feasible, but are frequently *ineffective* and *sometimes* produce fatal complications The *electric pacemaker*, on the contrary, is completely safe and is uniformly effective in terminating attacks due to slow idioventricular rates or ventricular standstill As soon as possible, therefore, the electric pacemaker should be attached to the patient and stimuli of increasing intensity applied until cardiac responses occur (Fig 11-47) If adequate intrinsic ventricular activity appears following resuscitation, stimulation may then be stopped However, if there is excessive delay in applying the cardiac pacemaker, or if the mechanism is ventricular fibrillation, these measures will fail

The author has now resuscitated over 200 patients from Stokes-Adams attacks with the electric pacemaker In an early series of 50 cases, attacks due to *very slow idioventricular rates* were observed in 12 patients, and to *ventricular standstill* in 45 patients; *these episodes of cerebral ischemia were all terminated immediately by electric stimulation.* This dramatic effect was observed countless times Stokes-Adams attacks due to *ventricular tachycardia or fibrillation were seen in 20 patients. It is clear that such seizures cannot be terminated by stimulation.* However, in 8 patients with frequent attacks due to multifocal ventricular tachycardia or fibrillation, *continued external stimulation prevented their recurrence.*

If adequate intrinsic ventricular activity fails to appear *after successful* resuscitation, a new, second *problem is posed. It has heretofore* been impossible to observe ventricular standstill for more than the few minutes that life *would persist.* For the first time, we have in the *electric pacemaker a means* of producing heart beats under such *circumstances and of* maintaining life indefinitely (as long as 109 hr *in the author's experience*). With the patient kept alive by the external pacemaker, there is no desperate *emergency*, and heroic and dangerous measures are unnecessary. With careful, deliberate *infusions of diluted solutions of sympathomimetic amines*, particularly *epinephrine hydrochloride*, the author was often successful in arousing an idioventricular *rhythm*, in accelerating it to an adequate rate, i.e, between 30 and 45 per minute, and in maintaining it there He *also used norepinephrine* to maintain an adequate blood pressure whenever necessary

The *prevention of recurring attacks* is a third major problem of Stokes-Adams disease that is still largely unsolved. When the idioventricular *rate is* too slow (below 30 *per* minute), *ephedrine sulfate* and *isoproterenol (Isuprel)* are often useful for long-term *maintenance* of heart rates *between* 30 and 45 beats *per minute*. When recurring attacks are due to varying *AV* conduction, *atropine*, *ephedrine*, and *isoproterenol* should be tried When the attacks are due to recurrent ventricular tachycardia *or* fibrillation, *ephedrine* and *isoproterenol* again, or the cardiac pacemaker, *may* be useful in *reducing* ectopic activity *by increasing* the basic ventricular rate;

"captures" may not take place. But in the same case, slight variations of the rates may produce a shift in the responsive and refractory phases, and *interference beats* may appear. Thus, the distinction of AV dissociation with or without interference is purely artificial.

The term AV dissociation is often loosely applied to AV heart block. AV heart block is due to depression or interruption of conduction, while in *AV dissociation*, the SA impulse fails to reach the ventricle because of its arrival during the normal refractory phase following a previous impulse (Katz, 1946).

Experimental Findings. Rothberger and Winterberg (1910, 1912) have shown that the development of AV nodal rhythm in dogs is preceded by a short phase in which the atria are controlled by the SA node and the ventricles by the AV node. In other experiments, occasional SA impulses interfered with the ectopic pacemaker. Ganter and Zahn (1912) obtained similar results. Scherf (1929) produced AV dissociation during aconitine intoxication. Luten (1925), in studies on digitalis intoxication in dogs, found that AV dissociation with a ventricular rate higher than the atrial rate preceded ventricular tachycardia. Van Bogaert (1933) arrived at similar conclusions with ouabain.

Clinical Findings. Wilson (1915) was the first to recognize AV dissociation with interference, and White (1916) described two further cases, to which another was added by Hewlett (1923). It was Mobitz (1923) who coined the term *interference dissociation*, which Scherf (1926) improved to *dissociation with interference*. Mobitz also gave a correct interpretation of the first case ever published but not recognized (Wenckebach, 1906). Lewis (1925) and Wenckebach and Winterberg (1927) published extensive reviews; these were brought up to date by Scherf and Schott (1953), Holzmann (1955), and Katz and Pick (1956).

Most cases were described in the course of acute rheumatic carditis, in which the incidence is about 10 per cent (Oettinger, 1935). Diphtheria (Korth and Schrumpf, 1936) and other acute infections may also cause it. Digitalis overdosage as well as acute infections were considered in the cases of Bloom and Perlow (1930), Laubry and Lequime (1933), and Laubry and Puddu (1936). Scherf and Boyd (1948) believe that dissociation with interference is rare in nondigitalized patients, but only 2 of the 12 cases of Cutts had digitalis. Quinidine sensitivity may also cause it (Linenthal et al., 1953). These factors often act in combination; simultaneous administration of quinidine and digitalis, operative trauma, anesthesia and digitalis—each was responsible in single cases of the author's series. It has also been observed with coronary heart disease and syphilitic aortitis, and exceptionally during hypertensive crises of adrenal tumors (Hegglin and Holzmann, 1937). While, in most of these cases, AV dissociation was transient, in a child of Ledoux and Arcay (1936) with a normal heart, it had been persisting for years. Since persistent AV dissociation was observed in association with atrial septal defect, it may exist as a congenital variety (Papp, 1957).

The diagnosis is made through the electrocardiogram. The clinical impression is that of atrial extrasystoles, since the interfering beats are premature and are not followed by a compensatory pause. The irregularity also disappears on effort, for SA acceleration may temporarily abolish AV dissociation. The venous pulse may show *giant waves* when atrial and ventricular contractions coincide. Coexistent SA bradycardia may cause syncope.

Electrocardiographic Patterns. The varying SA rate (if SA arrhythmia is present), the coexistence of latent or partial heart block, the tachycardia caused by an irritable AV node, the variations of the refractory period of the junctional tissues and the ventricles, the transition into AV nodal rhythm may cause most intriguing tracings of complex arrhythmias.

The *common pattern* of AV dissociation with interference is shown in Fig. 11-43A. The average atrial rate is 90 and, therefore, slower than the average ventricular rate at 110; there is SA arrhythmia, while the AV nodal rhythm, except for the beat following the conducted sinus impulse, is regular. The third to eighth and last ventricular complexes are transmitted to the ventricle with a normal P-R interval and are premature. Only P waves falling on top of the T wave (end of the refractory phase) are conducted. The two rates are so aligned that no P waves fall in late diastole and can reach the ventricle. The three conducted beats form the only link between the SA and AV nodal rhythms.

quinidine and *procaine amide* are contraindicated in these patients with heart block and Stokes-Adams disease.

It is for this reason that a clear distinction should be made between patients with AV block who have Stokes-Adams attacks and patients without AV block who may have disturbances of ventricular rhythm. Episodes of ventricular arrhythmias that cause cerebral ischemia in the latter patients should not be called Stokes-Adams attacks but rather *cardiac syncope*, a much more general term. In them, there is no contraindication to quinidine and procaine amide.

Despite all the author's efforts and this new approach, many of the patients have died of Stokes-Adams attacks. These fatalities occurred because the electric pacemaker was not applied during a fatal attack when the episode occurred unexpectedly; because the attack was due to ventricular tachycardia or fibrillation and was not terminated by the electric pacemaker; or because of irreversible cerebral damage due to delay in applying electric stimulation. Several patients died of complications of their Stokes-Adams disease or of other primary disease, such as acute myocardial infarction, acute bacterial endocarditis, cardiac tamponade from multiple cardiac punctures, and congestive heart failure

Episodes of cerebral ischemia due to *ventricular standstill or fibrillation* also occur in patients without Stokes-Adams disease Certain of these episodes, as in the carotid sinus syndrome, are usually transitory, and are clearly due to reflex vagal stimulation The distinction between Stokes-Adams attacks and reflex vagal standstill is of clinical importance because of differences in the course, prognosis, and treatment of each condition. Again, this distinction is usually simple but ultimately depends upon the presence or absence of AV block at any time between attacks

External electric stimulation was repeatedly effective in resuscitating three patients with ventricular standstill due to reflex vagal stimulation. In all of them, episodes of ventricular arrest repeatedly interrupted normal sinus rhythm abruptly, producing syncope and convulsions. The precipitation of such episodes by carotid sinus pressure and their disappearance following the administration of *atropine sulfate* established their reflex vagal origin. More than 100 times, in these patients, external electric stimulation terminated ventricular standstill and restored an effective circulation

A third type of cardiac arrest occurs as a result of *depression of cardiac automatism due to drugs*. The author has observed three patients with attacks of syncope due to digitalis. With digitalis toxicity, SA block occurred, whereupon cardiac activity was maintained by nodal or ventricular pacemakers, intermittent failure of these pacemakers resulted in periods of ventricular standstill lasting as long as 1 min. External electric stimulation resuscitated the patients several times. *With recession of* the digitalis effect, the seizures stopped.

Two patients with ventricular standstill following intravenous administration of procaine amide in the treatment of ventricular extrasystoles and tachycardia, have also been resuscitated promptly by other workers by means of the external electric pacemaker.

Cardiac arrest may also occur in a fourth group of patients. Young, healthy, individuals without heart disease may develop cardiac arrest unexpectedly, while undergoing various diagnostic and therapeutic procedures, particularly while *under anesthesia* in the operating room. Though infrequent, each such accident is a dreadful catastrophe.

The commonly recognized mechanisms of unexpected arrest are ventricular standstill or fibrillation, standstill is the usual cause, occurring probably about 90 per cent of the time, and reflex vagal stimulation appears to be a frequent precipitating factor.

Electric stimulation of the heart has been effective in 11 such cases of unexpected cardiac arrest Three of these patients were observed by the author personally. The others were described to him in personal communications by the physicians concerned The cases occurred during various procedures, 10 during surgery, 1 during pericardiocentesis The cardiac arrest was terminated in each case by the electric pacemaker, so that thoracotomy and cardiac massage were not necessary. Eight of the 11 patients recovered completely; 2 died of unsuccessful cardiac surgery, and 1 died 5 hr after an abdominal *operation*

The author's experiences with the cardiac pacemaker indicate that external electric stimulation can resuscitate the heart from arrest that occurs unexpectedly under anesthesia during

As soon as the SA rhythm slows, dissociation with interference appears During maximal deceleration, SA bradycardia at an average rate of 39 develops; a bigeminal rhythm consisting of a nodal escape and a conducted beat keeps the ventricular rate at 80 (Fig 11-44B). When the vagal effect subsides, SA rhythm is again restored (*last two cycles* of Fig 11-44C). The P waves, which appear at a distance of 0 26 to 0 37 sec after the nodal escapes, are conducted to the ventricles at a speed of 0 31 to 0 34 sec (Figs 11-43D, E, and 11-44) This may suggest a reciprocal rhythm. However, if the P waves are magnified through use of a right atrial lead and double amplification, it becomes evident that all P waves are upright and of SA origin, and that there is no retrograde conduction (Fig 11-43D, E). Even so, the reactivation of the SA node after the nodal escape suggests that the latter is instrumental in this, either through a mechanical effect (White, 1921, Rosenbaum and Lepeschkin, 1955) or by improvement of the circulation in the SA node If this is so, the two pacemakers also work in relay, the AV node reactivating the SA node and this then taking over the lead for a few beats until a longer SA standstill occurs which provokes a nodal escape

AV dissociation due to irritability of the AV node is rare and forms a link with paroxysmal tachycardia (Fig 11-45)

Contrary to Figs 11-43D, E, and 11-44, which show SA bradycardia, the basic disturbance is an *ectopic* atrial tachycardia at an average rate of 128 with 2:1 AV block and a P-R interval of *0 24 to 0.28 sec* (Fig. 11-45, bottom row). Slight slowing of the SA rhythm produces an AV nodal [illegible]), which [illegible], during [illegible] wo rates

soon equalize, slight slowing of the AV *rhythm* coincides with *slowing of the SA rhythm* (Fig. 11-45, top row), until a P wave falls late enough in diastole to capture the ventricles (sixth R wave). The dissociation, however, persists, even though the AV nodal rhythm has become slow; a P wave falling late in diastole remains blocked because of coexistent AV block. The same factors which produce an irritability of the SA node act on the AV node as well, which explains the alignment of the two rates during the tachycardic phase.

The association of 2:1 AV block with AV dissociation, but without nodal irritability, has a different electrocardiographic pattern. Conducted beats here have an aberrant pattern which appears when the SA rhythm slows. The ectopic center is emerging only when the half SA rate becomes less than the autonomic rate of the ectopic center. The number of impulses discharged by the SA node is of secondary

Fig 11-45 Lead II AV dissociation with "irritable" AV node. A. End of a *paroxysm with a conducted beat* AV dissociation persists The P wave before last is blocked in spite of its *late appearance in diastole* B Beginning of a nodal paroxysm with AV nodal escape (third beat) followed by gradual nodal acceleration until atrial and nodal *rates equalize* AV dissociation during paroxysm C Ectopic atrial tachycardia *with 2 1* AV *block, P-R* interval = 0 24 to 0 28 sec (Courtesy of Sir John Parkinson)

surgery or other procedures, just as it does from the other types of cardiac arrest The technique has been applied safely in the operating room within the few minutes available for complete resuscitation. It seems to us, therefore, that external electric stimulation of the heart should be tried quickly, even in the operating room, before resorting to thoracotomy and cardiac massage.

In addition to these successful experiences, the author has personally attempted resuscitation with the cardiac pacemaker unsuccessfully in several patients who developed unexpected cardiac arrest, most, but not all, of them during anesthesia A brief list of the procedures involved indicates *their wide variety and frequently* insignificant nature They include jugular puncture, intravenous pyelography, bronchography, cardiac catheterization, endotracheal intubation, hip nailing, cholecystectomy, and thoracic and cardiac surgery In a few, the circulatory arrest was due to ventricular *fibrillation, and stimulation was* ineffective In all the others, electric stimulation was applied too late, over 5 min after onset of arrest, and usually after prolonged, ineffective massage

These failures emphasize two critical problems of unexpected cardiac arrest First, the responsiveness of the heart to stimulation diminishes progressively with continued anoxia Second, effective ventricular beats *cannot* be stimulated by the pacemaker during ventricular fibrillation The time interval between arrest and the resumption of effective ventricular output must be brief, probably less than 3 or 4 min, if cerebral and cardiac function is to return unimpaired Avoidance of excessive delay depends upon immediate recognition of the cardiac arrest and then the immediate application of external stimulation and institution of a prearranged program for resuscitation

Immediate recognition of arrest at its onset depends upon continuous monitoring of cardiac activity The author has developed a practical *monitoring device* [2] combined with the pacemaker, and has used it to great advantage in the operating room and in patients with recurring Stokes-Adams attacks, to signal immediately the cessation of heart beats. Briefly, the monitor amplifies the electric activity of the heart like an electrocardiogram, so that patient contact and pickup of impulse are not difficult, *it gives an audible as well as a visual signal of each beat*, so that undivided attention to the monitor is not needed, and *it rings a compelling alarm* with the onset of arrest. Furthermore, it shows the mechanism of the arrest promptly, so that there is no problem in differentiating ventricular standstill from fibrillation If standstill is seen, stimulation with the pacemaking half of the machine can be effected without delay through the same electrodes on the chest. Ideally, perhaps, such a monitor-pacemaker should be *applied routinely to all patients under anesthesia.* Certainly the monitor-pacemaker should be applied beforehand to all patients undergoing anesthesia who present a particularly high risk of cardiac arrest. This specially vulnerable group includes patients with extreme debility, severe heart disease of any kind, AV block of *any degree, patients receiving large doses of* quinidine or procaine amide, patients with high serum potassium, patients with a sensitive carotid sinus, patients undergoing surgery involving the extraocular muscles, and particularly patients who have had previous episodes of cardiac arrest.

Immediately upon recognition of arrest, a rehearsed program of treatment should be instituted The heart should be stimulated mechanically by striking the precordium forcefully, by cardiac needle puncture, or by cardiac manipulation through the diaphragm, if *the abdomen is open* These measures are simple and immediately feasible and are worth the few seconds necessary because they are occasionally effective. If no time has been lost in the recognition of arrest, it is proper to spend no more than 1 min in attaching and trying the cardiac pacemaker. This trial, which should be successful in most cases of ventricular standstill, can be made easily within this time limit if the electric pacemaker is close at hand and if the operating room personnel have been trained in its use by previous emergency drills

If the initial mechanism of cardiac arrest is ventricular fibrillation or if the patient is not resuscitated by external mechanical or electric stimulation, the chest must be opened promptly and cardiac massage begun. At the

[2] Manufactured by the Electrodyne Company, Norwood, Mass.

11-43A) because of different spread of the SA impulse in the bundle. The P-R interval of the SA beats may be normal (Fig. 11-43A) or prolonged (Figs. 11-43, 11-44, 11-45). The prolongation may be due to latent heart block (long P-R interval), early conduction before complete recovery of the bundle takes place, or both. There is an inverse time relationship between the R-P *period and the P-R interval of the conducted beat* (Katz, 1946; Katz and Pick, 1956). The later the P wave appears in diastole, the faster is the AV conduction. In Fig 11-43E, the P waves appearing on top of, or shortly after, the preceding T wave are conducted to the ventricle at a speed of 0 30 or 0.32 sec, the P waves appearing later in diastole are conducted in 0 24 sec, which was the fastest conduction time of this patient, who had latent heart block. Latent heart block is frequently found in AV dissociation and is a predisposing factor, for impairment of forward conduction favors the development of retrograde block The distance between the conducted ventricular complex and the following AV nodal beat is usually the same as between two nodal beats, since nodal automatism is quickly restored (Figs. 11-43D, E, and 11-44), but it may be shorter (Fig 11-43A) or longer.

The shortening has been explained by Scherf and Schott (1953) by the late appearance of the SA beat because of delayed conduction in the bundle (see slight aberrance in Fig 11-43A) while the nodal beat is on time. If the distance is slightly prolonged, it is due to fatigue of the conducting system; if the pause *is longer and is equal to the distance between* a conducted P wave and the next nodal R wave, following a conducted ventricular complex, one has to assume that *concealed conduction* (Langendorf, 1948) has taken place. This means that the sinus impulse reached the AV node, destroyed the immature AV impulse, and was blocked on its way to the ventricles, so that it did not become electrically visible. The same phenomenon was earlier described by Korth (1941) as *incomplete interference*, and explained by Schott (1937) as a sign of impaired conduction in the bundle.

AV dissociation may appear as a *passive ectopic rhythm* through SA bradycardia or SA block, it can then be *temporarily* abolished by exertion (Fig. 11-44A).

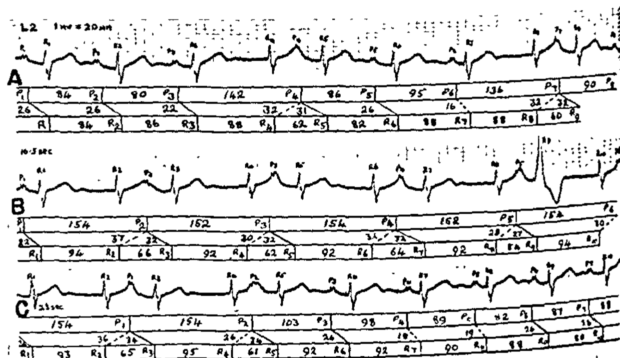


Fig. 11-44. Same case as in Fig 11-43D Lead II A. End of exercise test; after the fourth beat, incomplete AV dissociation B 16.5 sec after the end of (A). sinus bradycardia and bigeminal rhythm formed by a nodal beat and a conducted beat during maximal deceleration. R_9, which is early, shows aberrant conduction. C 23 sec after the end of (B), bigeminal rhythm gradually subsiding, conducted beats alternating with AV nodal beats in the second half of (C). Full lines, transmitted impulses; interrupted lines, no conduction. (Permission of the British Heart Journal.)

same time the anesthetist must provide adequate respiratory exchange of oxygen. Once blood is being squeezed out of the heart by the surgeon's hand, the desperate urgency of the 3-min time limit is over and further measures can be undertaken, if necessary, with more care and deliberation.

If the ventricular fibrillation appears or persists in spite of effective massage, *defibrillation* should be attempted only after the myocardium becomes pink and firm, *countershock* with a 60-cycle alternating current of 120 to 150 volts for 0.15 sec applied across large electrodes on the heart is most effective for this purpose.

Ventricular standstill may persist despite effective massage or may recur following defibrillation. *Epinephrine hydrochloride* (1 ml of a 1:10,000 dilution) may be injected into the left atrial chamber and may be repeated in 3 min if necessary. If standstill continues and the myocardium is flabby, 5 ml of 10 per cent *calcium chloride* may be given For persistent standstill, the electric pacemaker may be applied directly to the heart with a special bipolar electrode, so that massage need not be continued too long

If resuscitation is successful, the patient should be kept under constant observation for 2 or 3 days, because arrest frequently recurs. The cardiac monitor-pacemaker is most useful in providing continuous information about cardiac activity during this time and in providing immediately available, effective resuscitation from standstill. In the last year we have saved two patients from recurrent arrest in this way

The second mechanism by which cardiac arrest may occur is *ventricular fibrillation* Countershocks of 60-cycle alternating current of 50 to 150 volts and for 0 1 to 0 2 sec applied across the exposed heart have been used for some time as an adjunct to cardiac massage to stop ventricular fibrillation Recently the author and others have used similar countershock current of higher voltage experimentally to stop ventricular fibrillation by applying it *externally* across the unopened chest (Guyton et al.) The author has applied such high-voltage countershocks repeatedly in the experimental animal without producing damage to the heart, nervous system, or skin.

Furthermore, he found that externally applied countershock would also terminate atrial fibrillation, atrial tachycardia, nodal tachycardia, and ventricular tachycardia as well as ventricular fibrillation. The efficacy of the external countershock was clearly established by the repeated observation of the instantaneous cessation of these arrhythmias upon application of the electric current (Zoll, 1956c).

After these successful experimental observations, this technique was applied to ventricular fibrillation in man (Zoll, 1956b). The author has now stopped ventricular fibrillation twenty times in 11 patients. However, all but 1 of these patients died In each fatal instance the countershock was applied after considerable delay (5 min or more), and effective beats did not return after defibrillation. It was recognized beforehand in most of these cases that the procedure had little chance of saving the patient because of the long delay The underlying causes of fibrillation in these cases were acute myocardial infarction, digitalis intoxication, and Stokes-Adams attacks

One patient survived. He had active Stokes-Adams attacks and was resuscitated from many episodes of ventricular standstill by the electric pacemaker, and from three episodes of ventricular fibrillation by external countershocks of 270 to 360 volts. In each instance the countershock was applied within 3 or 4 min after the onset of the fibrillation Ventricular standstill occurred after each defibrillation, but external electric stimulation then evoked effective ventricular beats, which were followed shortly by an intrinsic ventricular rhythm and complete recovery. Figure 11-48 shows the electrocardiograms taken during one of these episodes In the last year, the author has successfully resuscitated 8 patients over 400 times from ventricular tachycardia or fibrillation by external electric countershock.

The termination of atrial fibrillation, supraventricular tachycardia, and ventricular tachycardia by external countershock, in addition to the possibility of external defibrillation, has wide clinical potentialities that have not been completely explored This technique may prove useful in desperate cases resistant to drug therapy, by providing a means of immediate termination of the arrhythmia without the dangers of prolongation of the arrhythmia and in those connected with massive drug administration.

ectopic beats is a multiple of a common denominator representing the cycle length of the ectopic rhythm. This can be easily calculated if two extrasystoles are seen in sequence; if they are separated from each other by longer stretches containing SA beats, the refractory period has to be determined on the basis of the shortest "coupling" separating the extrasystole from the previous SA beat. The latent beats have to fall within the refractory period, which may be much longer than the Q-T period, especially when the rate of both the SA and the ectopic pacemaker is slow. An example is shown in Fig. 11-46, where the SA rate is 43 and the ectopic rate is 34. The shortest "coupling" over long stretches of records was 0.76 sec (Fig. 11-46), all ectopic impulses following at a shorter distance after the previous SA impulse remain latent (interrupted vertical arrows). The parasystolic center shows more irregularity than usually observed—the cycles should not vary by more than 0.05 sec (Pick, 1953)—yet the varying "coupling" and the identical shape of extrasystoles make the diagnosis certain.

More than one parasystolic center may be active simultaneously (Holzmann, 1935); cases of atrial parasystole have also been described (Scherf and Schott, 1953). The parasystolic center may appear only intermittently when both rates are stable and so linked with each other that the ectopic impulses mostly fall during the refractory period. Carotid sinus pressure may suppress the SA rhythm, the parasystolic rhythm remaining in sole control (Mueller and Baron, 1953). Amyl nitrite in-

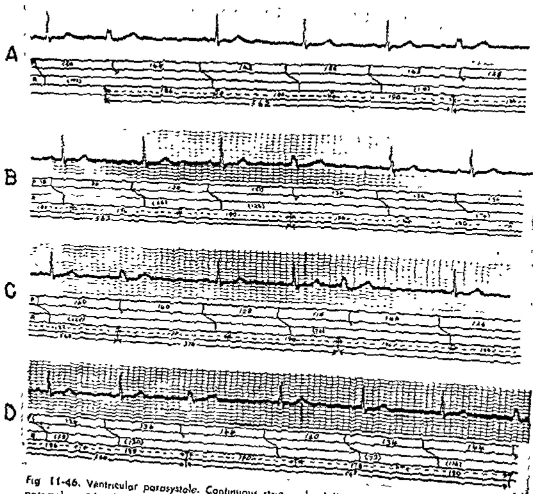


Fig. 11-46. Ventricular parasystole. Continuous strip in lead II. Sinus rate, 43, rate of ectopic pacemaker, 34. Shortest coupling of manifest ectopic beats (full vertical arrows), 0.76 sec. All ectopic beats falling short of this distance remain latent (interrupted vertical arrows). Horizontal interrupted lines, distances between ectopic impulses; horizontal full lines, distances between manifest ectopic impulses. Woman, aged 53; coronary disease.

The demonstrated efficacy of external coun-rshock in stopping ventricular fibrillation in an *provides a readily available* and safe tech-ique *for stopping this usually* fatal arrhythmia. *utside the operating* room and in seriously l patients in whom thoracotomy and cardiac assage may be *particularly* inadvisable, ex-rnal countershock may offer the only ef-ective therapy. In the operating room, con-nuous cardiac monitoring, immediate external lectric stimulation, and external electric de-ibrillation make up a combined technique y which unexpected cardiac arrest may be ecognized promptly, and the patient may be esuscitated from ventricular standstill or fi-rillation, before resorting to the more for-idable and traumatic procedure of cardiac massage

The major difficulty with external electric cardiac stimulation is that the electric shocks which stimulate ventricular responses are often very painful. Although this pain is not important in the emergency resuscitation of an unconscious patient from cardiac arrest, it *is* often very distressing when patients require prolonged or repeated *stimulation for repetitive seizures*, persistent absence of *intrinsic* ventricular beats, excessively *slow idioventricular* rates, or prevention of recurring ventricular tachycardia or fibrillation. These problems arise most in patients with Stokes-Adams disease, whether it occurs naturally from cardiac disease or whether it follows cardiac surgery, particularly the repair of interventricular septal defects.

Several approaches to this problem of pain with stimulation have been developed. In the first place, analgesic agents like *meperidine* (Demerol) often make the pain more tolerable. Furthermore, careful application of the electrodes to the chest wall with moderate rubbing of the skin may lower the threshold for

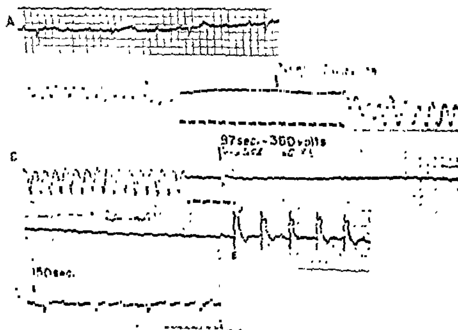


Fig 11-48 Resuscitation from ventricular fibrillation in a *patient with Stokes-Adams* attacks. Lead aVF, amplification half-normal (1 mv = *5 mm*). *A. Patient's usual idioventricular rhythm* before seizure B Ventricular fibrillation that *persisted after application* of countershock of 300 volts The indicated *times are from the beginning of the continuous electrocardiogram*, 1 min *after the episode* began The broken line indicates when the *electric activity* of the heart was *not being* recorded ("instomatic" *switch turned on*) *C. The two* strips are continuous External countershock of 360 volts at 87 *sec terminated the arrhythmia* and produced ventricular standstill External electric stimuli, E, at 60 volts *produced* ventricular beats, V, 12 sec later. *D. Resumption* of usual idioventricular *rhythm within a* few seconds after termination of electric stimulation. The patient regained *consciousness promptly* and recovered completely. *(From Zoll, New England J. Med* 1956)

importance; it is the number of impulses reaching the bundle which determines the activity of the secondary pacemaker (Oettinger, 1935; Dressler et al., 1952).

Transition from AV dissociation to AV nodal rhythm is not uncommon (Fig. II-43B); the two arrhythmias are interrelated, and the difference consists only in the presence or absence of retrograde block AV dissociation may also appear as a transient phase under quinidine treatment for atrial fibrillation before SA rhythm is established. It is often observed during acute rheumatic fever in combination with almost any arrhythmia (Bain, 1939; Vakil, 1954).

Prognosis and Treatment. *Prognosis* depends on the underlying cause. AV dissociation has little significance if it appears in a patient with otherwise healthy myocardium, but this is rarely the case. Its appearance during infections means cardiac injury, which may be slight or severe, its persistence after subsidence of rheumatic arthritis is a warning that carditis is still active Should it develop during treatment with digitalis or quinidine, the drugs should be stopped, for the disturbance is evidence of toxicity

Treatment has no place in AV dissociation. When the latter arises as a passive ectopic rhythm, it is an expression of a normal cardiac mechanism brought into play by depression of primary impulse formation Syncopal attacks due to SA bradycardia cease as soon as nodal automatism is established. If AV dissociation is due to nodal irritability, treatment should be that of paroxysmal tachycardia.

PARASYSTOLE

Parasystole, like AV dissociation, involves the concept of two simultaneously and independently acting pacemakers, one of which is in the SA node, the other usually in one of the ventricles. Such a possibility was first shown to exist by Fleming (1911) He imagined that the ectopic focus lies in "what may be called a backwater of primitive cardiac tissue" and that "physiological stimuli passing down the main channel are unable to disturb the point where ventricular stimuli arise", thus, the slower ventricular focus remains protected from the faster SA impulse. A *protective block* was assumed by Kaufmann and Rothberger (1919), who later (1922) made the first extensive study of the coexistence of two independent centers of impulse formation. In cases with ventricular rhythm faster than that of the SA pacemaker, it was thought that there might be an *exit block* which prevents the dominance of ectopic pacemaker and the transformation of parasystole into ventricular tachycardia. The term "block" applied in this sense is a misnomer, for the emphasis is not on inhibited conduction but on diminished excitability; excitability in relation to strength of the dominant rhythm determines the function of the ectopic center (Scherf and Chick, 1951).

Scherf (1927) was able to produce short periods of parasystole in dogs by mechanical and electrical stimuli after reduction of cardiac excitability with quinidine or sensitization of the heart with barium chloride and aconitine Longer-lasting parasystole, without mechanical stimulation, was produced by application of veratrine; parasystole so produced fulfilled most of the clinical criteria.

Parasystole is rare, its incidence being about 0 04 per cent of all routine ECGs recorded in a general hospital (Scherf and Boyd, 1950). It is mainly observed in coronary heart disease and is believed to be always evidence of an abnormal heart, except for the exceptional cases of nodal parasystole (Pick, 1953). Whether this belief can be upheld is questionable, since cases with normal hearts have been described (Singer and Winterberg, 1920, Heinz and Eldridge, 1957). Scherf and Schott (1953) found 11 cases without structural heart disease among 49. Most of the patients with organic heart disease were experiencing heart failure and were receiving digitalis, stopping the drug abolished the ectopic rhythm (Holzmann, 1935).

Electrocardiographic Patterns. The common electrocardiographic pattern is that of ventricular extrasystoles of identical shape. These appear at a varying distance from the SA beat and, therefore, are not induced by it, the "coupling" is variable, as opposed to the usual form of extrasystole to be observed in bigeminal rhythm. In fact the term "coupling" should not be applied, since the ectopic beats appear as cycles of an automatic rhythm, the emergence of which is regulated by the refractory phase of the dominant rhythm. When SA and ectopic impulses fall together, fusion beats result, having an intermediate shape between ectopic and SA beats. The final proof of parasystole can be given if the distance between two

stimulation with consequent reduction in the amount of pain.

A second approach has proved most useful in the management of atrioventricular block and cardiac arrest that follow cardiac surgery and constitute a major complication of open-heart surgery. A modification of the technique of external electric stimulation of the heart was introduced (Weirich et al., 1958), by *stimulating the heart directly* with an electric pacemaker. At the time of surgery, a wire is inserted into the myocardium and brought through the skin, where it is attached to an electric stimulator, and a second wire from the pacemaker is placed subcutaneously to complete the electric circuit. Effective cardiac stimulation is possible by way of the myocardial electrode at voltages (usually well below 10 volts) that do not produce any pain or skeletal muscular movement. This type of direct cardiac stimulation can be used freely and most effectively in the management of postoperative heart block for several weeks after surgery; in most instances, during this time, normal sinus rhythm returns and the difficulty is completely solved. In addition to the requirement of open thoracotomy to place the electrode, this technique does have two limitations. Infection may occasionally occur at the site of exit of the wires through the skin. Secondly, stimulation via the myocardial electrode becomes ineffective, usually within 8 weeks or less, apparently because of inflammatory reaction about the myocardial electrode. These difficulties make this method unsuitable for the long-term management of patients with Stokes-Adams disease.

Two interesting modifications of Lillehei's direct myocardial stimulation have been introduced to obviate the necessity for thoracotomy. One has been the introduction of a myocardial electrode by Thevenet et al. (1958) through a blind percutaneous puncture. This technique carries with it the risk and uncertainty of a blind puncture of the heart plus the original limitations of cutaneous infection and ultimate ineffectiveness of stimulation within a month or two.

The second modification, by Furman and Schwedel, is the introduction of an *intracavitary wire electrode* by way of a cardiac catheter passed up a vein of the forearm into the right ventricle. Direct cardiac stimulation at voltages less than 10 volts without pain was carried out by him in one patient with Stokes-Adams disease for over 3 months. Local skin infection is a problem with this technique also, but effective stimulation is apparently possible for longer periods than with the myocardial electrode. The additional possible complications of thromboembolism and trauma to the right-sided endocardium or valves were not encountered, anticoagulant therapy was maintained throughout the entire period of stimulation. This procedure is clearly most useful in patients with Stokes-Adams disease with persistent seizures, who cannot tolerate external electric stimulation. Under these circumstances, the risks of the procedure are clearly acceptable. It is equally clear, however, that this technique cannot be used indefinitely for the permanent maintenance of patients with Stokes-Adams disease throughout their lifetime. Better techniques of management, by pharmacologic agents or by electronic pacemakers that may be buried in the body and operate effectively and indefinitely, are under investigation for this ultimate goal.

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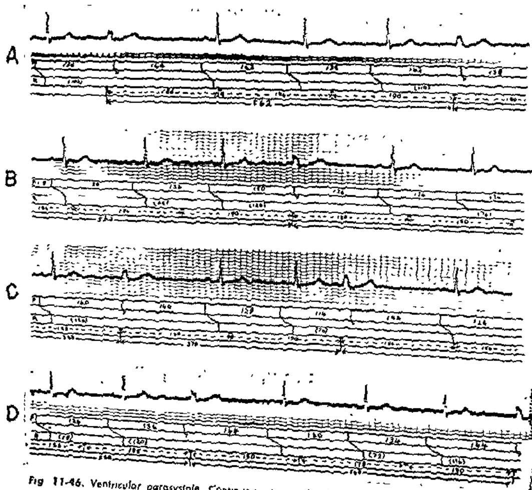


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Clinical differentiation of cardiac arrhythmias

RUSTOM JAL VAKIL

Nomenclature. The term *normal sinus rhythm* implies a regular rhythm of from 60 to 100 beats per minute, initiated at the SA node. Any deviation from normal has been referred to as *cardiac arrhythmia*, irrespective of whether the abnormal rhythm was regular or irregular. Such a procedure of labeling a perfectly regular rhythm, such as that of complete heart block, paroxysmal tachycardia, sinus bradycardia, or atrial flutter, as "cardiac arrhythmia" is definitely unscientific. Hence, arises the need for more scientific designations, such as abnormal heart rhythms, abnormal cardiac mechanisms, *disorders of the heart rhythm*, or dysrhythmias.[1]

Importance of Abnormal Heart Rhythms. Abnormal heart rhythms are of clinical importance for several reasons: (1) their incidence is high in clinical practice, (2) they are a source of anxiety to both patient and doctor, (3) they often focus attention on the correct diagnosis of the disease, (4) their diagnosis is often an essential prerequisite to successful treatment, (5) they may predispose to complications or untoward events, (6) they may alter the prognosis or outlook of an existing cardiac condition, and (7) their prompt treatment may postpone or avoid the occurrence of cardiac failure.

Anatomicophysiologic Considerations. From early embryonic life until death, the conducting system of the heart has the power of automatic and rhythmic contraction. The conducting system is a specialized neuromuscular tissue, endowed with the power of initiating and conducting cardiac impulses.

The heart beat is normally initiated by the SA node, which, in normal conditions, has an inherent rate of stimulus formation greater than that of any other component of the conduction system. It is, therefore, referred to as the pacemaker of the heart; in the event of its being depressed or diseased, a subsidiary or secondary pacemaker takes over the function of initiating beats (nodal or idioventricular pacemaker).

CLASSIFICATION

Many different classifications of cardiac arrhythmias have been proposed from time to time, with alleged advantages, and later abandoned in favor of new ones. On the basis of the mechanisms involved, abnormal cardiac rhythms were classified into two major groups, viz., (1) disturbances of impulse formation (inclusive of various types of sinus or normotopic and ectopic or heterotopic rhythms), and (2) disturbances of impulse conduction (inclusive of sinoatrial, atrioventricular, and intraventricular blocks) by Vakil and Golwalla (1952).

The following classification of abnormal cardiac mechanisms or rhythms, recently proposed by the American Heart Association and based

[1] In order to avoid this confusing terminology, Luisada (1948) suggested dividing these disturbances into (a) tachycardias, (b) bradycardias, and (c) arrhythmias. The complex of these disturbances be called "disturbances of the heart rate and rhythm."

halation may have an opposite effect through acceleration of the SA rhythm or improved blood supply (Holzmann, 1935).

Parasystole with exit block is said to exist when only some of the ectopic beats falling outside the refractory period become manifest. This usually happens in the rare cases where the rate of the ectopic centers is faster than that of the SA rhythm.

Though parasystolic rhythm should be strictly separated from bigeminal rhythm with fixed coupling, intermediate cases have been described. Holzmann believes that the same metabolic state of the cardiac muscle induced by digitalis can cause reentry and parasystole; constant coupling can be simulated by stability of the two rhythms. In the case of Mueller and Baron, coupled rhythm alternated with parasystole, and the authors believed that the ectopic impulses were not strong enough to emerge except during the supernormal phase of recovery. The reverse, i.e., the production of induced extrasystoles by the ectopic pacemaker, has also been described (Scherf and Schott, 1951) and explained by "*directional*" *block* around the ectopic center.

Parasystole is an electrocardiographic curiosity and not a clinical state, since it has no hemodynamic importance. Prognosis and treatment depend on the causative factors.

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A second approach has proved most useful in the management of atrioventricular block and cardiac arrest that follow cardiac surgery and constitute a major complication of open-heart surgery. A modification of the technique of external electric stimulation of the heart was introduced (Weirich et al., 1958), by *stimulating the heart directly* with an electric pacemaker. At the time of surgery, a wire is inserted into the myocardium and brought through the skin, where it is attached to an electric stimulator, and a second wire from the pacemaker is placed subcutaneously to complete the electric circuit. Effective cardiac stimulation is possible by way of the myocardial electrode at voltages (usually well below 10 volts) that do not produce any pain or skeletal muscular movement. This type of direct cardiac stimulation can be used freely and most effectively in the management of postoperative heart block for several weeks after surgery, in most instances, during this time, normal sinus rhythm returns and the difficulty is completely solved. In addition to the requirement of open thoracotomy to place the electrode, this technique does have two limitations Infection may occasionally occur at the site of exit of the wires through the skin. Secondly, stimulation via the myocardial electrode becomes ineffective, usually within 8 weeks or less, apparently because of inflammatory reaction about the myocardial electrode. These difficulties make this method unsuitable for the long-term management of patients with Stokes-Adams disease

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12

Cardiac resuscitation by external electric stimulation and countershock

PAUL M. ZOLL

Cardiac arrest presents a critical problem in many different clinical situations It is a desperate emergency that requires prompt, energetic, and effective measures to effect resuscitation within the urgent time limit of about 4 min

Therapeutic procedures in the past have included cardiac puncture, intracardiac injection of drugs, and thoracotomy with cardiac massage, but the results with all these procedures are unsatisfactory in that the complete recovery rate is usually about 30 per cent (Stephenson et al, Cole)

A complicating factor in the emergency treatment of cardiac arrest is that the mechanism of the arrest may be either ventricular standstill or ventricular fibrillation These mechanisms cannot be differentiated by the usual clinical means but only by an electrocardiogram or by direct inspection of the exposed heart, they tend to occur in somewhat different situations, however, and, most important, they require different treatment

Ventricular standstill occurs particularly in four clinical situations, (1) in the Stokes-Adams attacks which occur in patients with AV heart block, (2) during reflex vagal stimulation, as in patients with a hypersensitive carotid sinus, (3) during treatment with cardioactive drugs, such as digitalis, quinidine, and procaine amide, and (4) unexpectedly, during various diagnostic and therapeutic procedures, particularly in the operating room under anesthesia *Ventricular fibrillation* may occur in a Stokes-Adams attack, but it occurs most often as a disastrous complication of acute myocardial infarction.

The first problem to be considered in this chapter is ventricular standstill. Recently, the author has developed a new therapeutic approach to the problems posed by it. It is an *externally applied cardiac pacemaker* that produces effective ventricular beats, terminates ventricular standstill, and maintains an externally controlled rhythm for as long as necessary until spontaneous ventricular beats return. The electric stimulator functions like a natural intracardiac pacemaker but is under complete external control (Zoll, 1952). Figure 11-47 shows the electrocardiogram of a period of cardiac arrest terminated by electric stimuli and ventricular beats. The instrument[1] is easily applied and clinically practicable Two dials permit variation of rate of stimulation, and of amplitude of stimulation from 0 to 150 volts. Output wires carry the electric stimuli to the electrodes, which are smeared with conductive jelly and held on the precordium (usually in the V_2 and V_5 positions) by plastic handles or a rubber strap. The electric shocks go through the chest wall and produce ventricular beats This technique of external electric stimulation of the heart has now been used successfully by the author and others to resuscitate over 200 patients with Stokes-Adams attacks, 3 with reflex vagal stimulation, 4 with standstill due

[1] Manufactured by the Electrodyne Company, Norwood, Mass.

cardia most often occur in subjects under 40 years of age, those of ventricular tachycardia are more common after 40. Complete heart block, although usually found in persons over 50, may be noted in childhood, when its origin is congenital, diphtheritic, or rheumatic. Premature ... may occur at any age, although

mitral disease or thyrotoxicosis, is more common ... females

bladder disease, chronic gastrointestinal disorder, or renal calculus is in favor of extrasystole. A history of coronary occlusion or precordial pain suggests the possibilities of ventricular extrasystoles, ventricular tachycardia, or AV block

DRUGS AND ADDICTIONS Overdigitalization may provoke extrasystoles, especially with a bigeminal type of sinus bradycardia, sinus arrhythmia, or AV block Long-standing or excessive administration of epinephrine or ephedrine for bronchial asthma, of thyroid extract for obesity, or of atropine, quinidine, or barium chloride may elicit extrasystoles, sinus tachycardia, or AV block Excess of tea, coffee, or tobacco may be responsible at times for troublesome arrhythmias.

Specific Interrogation. PRECIPITATING FACTORS Ventricular extrasystoles, heart block, ventricular tachycardia, and sinus tachycardia are common after myocardial infarction, sinus bradycardia, sinus tachycardia, and disturbances of conduction are often observed during or after diphtheria, influenza, pneumonia, mumps, or jaundice Extrasystolic beats and paroxysms of supraventricular tachycardia may accompany gastrointestinal or emotional disorders

ONSET The onset of arrhythmia is dramatically sudden or instantaneous in paroxysmal tachycardia (especially supraventricular), it is gradual in sinus tachycardia, and at times in ventricular tachycardia, in the last, it may be preceded by premature contractions

ASSOCIATED SYMPTOMS An abnormal cardiac rhythm may be asymptomatic or may be associated with one or more symptoms. Palpitation is the most common symptom of all and is frequently noted with extrasystoles, atrial fibrillation, paroxysmal tachycardia, and sinus tachycardia A disagreeable thump or thud, when described after a pause, suggests a postextrasystolic beat Episodes of convulsions, associated with loss of consciousness and cyanosis (Stokes-Adams attacks), are suggestive of AV block. Polyuria, or frequency during attacks, suggests paroxysmal tachycardia Yawning, sighing, and a feeling of exhaustion are commonly associated with the sinus tachycardia of neurocirculatory asthenia and cardiac neurosis. A sense of fullness in the neck, occurring intermittently, is an uncommon manifestation of extrasystolic beats and is due to regurgitation of blood from the right atrium to the jugular veins Dizziness or faintness may occur during attacks of paroxysmal tachycardia or "runs" of extrasystolic beats. Severe precordial pain may arise during a prolonged attack of paroxysmal tachycardia

TERMINATION OF ATTACK. The termination of attacks is gradual in sinus rhythms and is usually sudden in paroxysmal supraventricular tachycardia When an attack is stopped by stooping or bending down, holding of the breath, or mechanical stimulation of the vagus nerve, supraventricular paroxysmal tachycardia is likely

Pulsatory Phenomena. HEART RATE. Since in

by auscultation at the apex, not at the wrist. Cardiac rates of below 40 beats per minute suggest either complete or severe incomplete AV block or nodal rhythm; regular rates of over 160 favor paroxysmal tachycardia. Sinus tachycardia and atrial flutter are usually associated with rates below 160 per minute. A persistent, regular, and unvarying cardiac rate of about 150 per minute, particularly in an elderly subject, suggests a 2:1 atrial flutter.

PULSE DEFICIT When the cardiac rate, determined at the apex, exceeds that of the radial pulse rate by 10 beats or more, a diagnosis of atrial fibrillation is justified. A pulse deficit, however, may also arise with ventricular extrasystoles, provided the pulses of the ectopic beats are too feeble to be conveyed to the radial pulse.

JUGULAR PULSE. Neck vein pulsations are of great diagnostic value, especially when studied in conjunction with the arterial pulse. For in-

resultant pressure hypertrophy of the left ventricle. The hypertension is related not only to the resistance of the coarctation, but also to a renal factor. There is an anatomic subclinical type without hypertension.

INFANTILE TYPE In this form, there is a diffuse *narrowing of the isthmus of the aorta,* which may involve the ostium of the left subclavian artery (short type) or the entire arch from the origin of the innominate (long type) (Fig 6-10A). Rarely, there may be complete absence of the arch Associated with this, there is always a widely *patent ductus arteriosus* and right ventricular hypertrophy. The ascending aorta is smaller than normal, but not so small as the coarctated area (see Chap 1).

Complexes Associated with Isolated Patent Ductus Arteriosus. In the usual complex (Burchell, 1946, Gross and Longino, Gordon et al.), the left atrium and ventricle are hypertrophied (Fig 6-10B) In long-standing cases, the right ventricle may also be hypertrophied, but the left ventricle dominates. In a few cases, the right ventricle is dominantly or exclusively hypertrophied. All the above complexes may be associated with a mild coarctation, bicuspid aortic valve, or subaortic stenosis All, likewise, show pulmonary arterial dilatation with sclerotic changes in the pulmonary artery and valve

PATHOGENESIS OF THE COMPLEX. In the usual case, there is a shunt from the aorta into the pulmonary artery, resulting in increased pulmonary flow Hence, the left atrium and ventricle present a volume hypertrophy. Eventually, *pulmonary hypertension* may develop due to pulmonary vascular changes resulting in bidirectional or reversed flow In a few cases, severe pulmonary hypertension occurs before puberty or shortly after birth, associated with reverse flow in the ductus These cases are not well understood

Complexes Associated with Isolated Atrial Septal Defect and Lutembacher's Complex. Atrial septal defects (Blount et al, 1956, Dexter, Taussig et al., 1938) may be classified as (1) patent foramen ovale, (2) persistent ostium primum, and (3) defects in other parts of the atrial septum A *patent foramen ovale* (Fig 6-11A) consists of an opening in the region of the *fossa ovalis.* When this opening is a direct communication between the atria, it represents a true functional atrial septal defect, permitting a bidirectional shunt. It may, however, be an obliquely oriented foramen guarded by the *septum primum* acting as a valve This type of opening becomes functional if the pressure in the right atrium exceeds that in the left. A





Fig 6-10 A Fetal coarctation complex. *A*, ascending aorta, *I*, isthmus, *D*, ductus arteriosus. B Potent ductus arteriosus Usual type Probe passes through the ductus *P*, pulmonary artery; *A*, aorta; *LV*, left ventricle. (B. From M. Lev *Autopsy Diagnosis of Congenitally Malformed Hearts.* Charles C Thomas, 1953)

small, nonfunctioning obliquely probe-patent foramen ovale is present in 20 to 25 per cent of normal hearts. A *persistent ostium primum* (Fig. 6-11B, C) consists of an opening in the lower part of the atrial septum, just proximal to the mitral and tricuspid valves. This opening is always of pathophysiologic importance.

In complexes associated with atrial septal defect, there is always right atrial and right ventricular hypertrophy and dilatation and dilatation of the pulmonary artery The left atrium and ventricle are normal or small This is the picture in the *secundum* type of defect. In the *primum* type of defect, there is usually a cleft anterior leaflet of the mitral and sometimes a cleft septal leaflet of the tricuspid. Here there may be left ventricular hypertrophy

PATHOGENESIS OF THE COMPLEXES The right atrium and ventricle, in these complexes, present a volume hypertrophy There is a markedly increased pulmonary flow The left ventricle is small because of the left-to-right shunt at the atrial level In the primum type of complex, there may be an associated mitral regurgitation, accounting for the left ventricle hypertrophy. When there is tricuspid regurgitation, there is an increased amount of volume hypertrophy of the right atrium and ventricle

Complexes Associated with Isolated Ventricular Septal Defect. Isolated defects of the ventricular septum (Selzer, Wood et al.) are found mostly in the region of the *pars membranacea,* involving the adjacent anterior and posterior septa (Fig 6-12). They may, however, also be found in the anterior or, uncommonly, in the posterior septum. These defects may be single or multiple The complex created by this defect is dependent upon its size When small, the shunt is not large enough to produce hemodynamic effects When large, the right ventricle is hypertrophied, and the left ventricle may or may not be hypertrophied. All such defects may have the following complications. (1) the aortic valve may be deformed or pulled down to produce aortic insufficiency; (2) the bundle of His may be involved by fibrosis to produce AV block; (3) the tricuspid valve may become adherent to the defect to produce tricuspid insufficiency, and (4) there may be superimposed bacterial endocarditis.

PATHOGENESIS OF THE COMPLEX. The right ventricle presents a volume and pressure hypertrophy, the shunt being from the left to the right ventricle. There is increased pulmonary flow and, hence, hypertrophy of the left atrium The left ventricle is subjected to opposite influences The increased volume leads to hypertrophy, while the decreased peripheral resistance leads to atrophy Hence the left ventricle presents a variable picture. In general, in the early stages of the process, it is hypertrophied and in the latter stages, normal or atrophied

Complex Associated with Common Atrioventricular Orifice. In this complex (Gunn and Dieckmann, Rogers and Edwards), there is one undivided AV orifice and one valve (Fig 6-13A) This valve consists of an inferior leaflet on each side, and a common posterior leaflet made up of the medial leaflet of the tricuspid and the posterior portion of the anterior leaflet of the mitral, an anterior leaflet on the left side made up of the anterior half of the anterior leaflet of the mitral, and an anterior leaflet on the right side representing the true anterior tricuspid leaflet The latter two may be fused



... Arrow points ... C Left atrial ... and ventricle ... to the defect.

on the site of origin and nature of the mechanism involved, has been more or less universally accepted of late:

ABNORMAL CARDIAC MECHANISMS OR RHYTHMS

1. Sinus Mechanisms
   1.1 Sinus Tachycardia
   1.2 Sinus Bradycardia
   1.3 Sinus Arrhythmia
   1.4 Sinus Arrest (Sino-atrial Block, Sinus Pause)
2. Atrial Mechanisms
   2.1 Atrial Premature Systole
   2.2 Atrial Tachycardia
   2.3 Atrial Flutter
   2.4 Atrial Fibrillation
   2.5 *Wandering Pacemaker*
3. Atrioventricular (A-V Nodal Mechanisms)
   3.1 Atrioventricular (A-V) Nodal Premature Systole
   3.2 Atrioventricular (A-V) Nodal Rhythm
   3.3 Atrioventricular (A-V) Nodal Tachycardia
   3.4 Atrioventricular (A-V) Nodal Escape
   3.5 Supraventricular Tachycardia
4. Ventricular Mechanisms
   4.1 Idioventricular Rhythm
   4.2 Ventricular Escape
   4.3 Ventricular Premature Systole
   4.4 Ventricular Tachycardia
   4.5 Ventricular Fibrillation
5. Parasystole
   5.1 Atrioventricular (A-V) Dissociation with Interference
   5.2 Other Parasystolic Rhythms
6. Mechanisms of Undetermined Origin
   6.1 Premature Systole of Undetermined Origin
   6.2 Tachycardia of Undetermined Origin
7. Atrioventricular (A-V) Conduction
   7.1 Incomplete A-V Block (Prolonged A-V Conduction Time)
   7.2 Incomplete A-V Block with Dropped Beats
   7.3 Complete A-V Block
8. Intraventricular Conduction
   8.1 Delayed Intrinsicoid (RS) Deflection, Left
   8.2 Delayed Intrinsicoid (RS) Deflection, Right
   8.3 QRS Interval, Prolonged
   8.4 QRS Interval, Prolonged, Intermittent
   8.5 Bundle-branch Block, Left
   8.6 Bundle-branch Block, Right
   8.7 Intraventricular Block, Unclassified
   8.8 Intraventricular Block, Intermittent
   8.9 Anomalous Atrioventricular Excitation

STUDY OF ARRHYTHMIAS

Nowhere, in the entire field of cardiology, has electrocardiography been exploited to greater advantage than in the interpretation of cardiac arrhythmia. The exact mechanism of many a *hitherto obscure irregularity of the* heart has been unraveled by resort to this method of instrumental investigation. Although the prime role of electrocardiography in the diagnosis of abnormal cardiac rhythms and its unquestioned superiority over other methods of examination have been securely established in recent years, the informative value of a good history and thorough clinical examination in the understanding of cardiac arrhythmias has not been sufficiently appreciated. Since the subject of electrocardiographic interpretation of cardiac irregularities has been dealt with at great length in various chapters of Vol. III of *Cardiology*, the present paper deals with the clinical differentiation only. The majority of cardiac arrhythmias, as a matter of fact, are clinically recognizable, provided a systematic method of cross examination or history taking and thorough physical examination are undertaken.

The following scheme of investigation, having proved valuable in the majority of cases, is recommended for routine adoption:

I. History
   A. General (age, sex, predisposing factors, etc.)
   B. Specific (regarding the various characteristics of the cardiac arrhythmia itself, e.g., onset, duration, associated symptoms, and cessation of attack)
II. Physical examination
   A. Observations of pulsatory phenomena
      1. Cardiac rate and rhythm
      2. Arterial pulse
      3. Venous pulsations
   B. Examination of the heart
      1. Presence or absence of organic heart disease
      2. Apex beat
      3. Heart sounds
   C. Special methods of clinical examination
      1. Effect of exercise
      2. Effect of deep respiration and of apnea
      3. Effect of carotid sinus pressure
      4. Levine's method
   D. Examination of other systems
III. Instrumental investigation
   A. Fluoroscopy
   B. Electrocardiography
   C. Phonocardiography

General Interrogation. AGE. While certain arrhythmias, such as sinus arrhythmia, paroxysmal supraventricular tachycardia, and atrial extrasystoles, are common in the young, paroxysmal ventricular tachycardia, ventricular extrasystoles, and atrial flutter show a predilection for elderly subjects. Sinus arrhythmia is common in infants, children, and the aged. Attacks of supraventricular paroxysmal tachy-

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breath may remove the irregularity of sinus arrhythmia, bring out latent extrasystoles, and help in the differentiation of pulsus paradoxus from pulsus alternans.

CAROTID SINUS STIMULATION. COMPRESSION OF THE EYEBALLS. These maneuvers have no effect on ventricular rate in complete heart block, atrial fibrillation, or ventricular tachycardia, they tend to cause further slowing of the heart rate in incomplete AV block, they frequently terminate an attack of paroxysmal supraventricular tachycardia, they bring about a gradual and transitory slowing of the heart rate in sinus tachycardia, they may cause a sudden halving of the rate in atrial flutter, even though, in most cases, they have only a moderate and temporary effect, particularly if there is variable block.

LEVINE'S METHOD "Tapping of the foot in rhythm with the heart" has been recommended by Levine as a useful method of differentiating supraventricular from ventricular tachycardia (even a slight irregularity of rhythm favoring the latter), atrial from ventricular extrasystoles (the postextrasystolic pause being strictly compensatory in the latter), SA from partial AV block (the pause, in the latter, does not correspond in length to two cardiac cycles), and atrial fibrillation from multiple extrasystoles (all pauses in the latter are preceded by small and rapid pulsations, i e , premature beats)

Instrumental Investigations. FLUOROSCOPY Fluoroscopy may afford diagnostic clues in arrhythmias Rapid and irregular undulations of the atria without proper contractions may be observed in atrial fibrillation Synchronous contraction of the atria and ventricle, with additional contractions of the atria during the long diastolic pauses, is suggestive of AV block. In atrial flutter, rapid and regular contractions of the atria may be visible in the right anterior oblique position

ELECTROCARDIOGRAPHY This method is capable of supplying information of immense diagnostic value and should be employed in every single case of cardiac arrhythmia; however, in many cases it serves only to confirm or exclude the diagnosis, after all clinical sources of information have been fully used.

CLINICAL CLASSIFICATION OF CARDIAC ARRHYTHMIAS

The following eight types of cardiac arrhythmias are recognizable clinically, on the basis of rhythm, rate, and perceptibility of cardiac pulsation (Vakil, 1954)

1. Regular rhythm with slow rate (rhythmic bradycardia)
2. Regular rhythm with rapid rate (rhythmic tachycardia)
3. Regular rhythm with normal rate
4. Regular rhythm with unequal force of beats
5. Irregular rhythm with slow rate (arrhythmic bradycardia)
6. Irregular rhythm with rapid rate (arrhythmic tachycardia)
7. Irregular rhythm with normal rate
8. Clinically silent (imperceptible) rhythm

Type I: Regular Rhythm with Slow Rate (1) Sinus bradycardia, (2) nodal rhythm, (3) incomplete (2:1 or 3:1) AV block, (4) complete AV block, (5) atrial flutter with 4:1 or 5:1 block, (6) atrial fibrillation with nodal rhythm.

A clinical diagnosis is possible, in the majority of cases, by simultaneous study of radial artery and jugular vein pulsations, and by palpation and auscultation of the heart.

Type II: Regular Rhythm with Rapid Rate. (1) Sinus tachycardia, (2) paroxysmal supraventricular tachycardia, (3) paroxysmal ventricular tachycardia, (4) 2:1 type of atrial flutter, (5) preexcitation (Wolff-Parkinson-White) syndrome.

A clinical diagnosis is facilitated by paying attention to the following features: (*a*) past history of similar attacks, (*b*) mode of onset of arrhythmia, (*c*) mode of termination, (*d*) duration of attack, (*e*) rate of beating, (*f*) rhythm, (*g*) venous pulsations of the neck, (*h*) influence of exercise, respiration, carotid sinus pressure, and posture.

Type III. Regular Rhythm with Normal Rate. A regular rhythm with a normal rate of 70 to 80 beats per minute need not necessarily imply a normal sinus rhythm, as certain pathologic mechanisms are compatible with such a state. (1) first-degree AV block, with increased AV conduction time, (2) intra-atrial block, (3) intraventricular conduction defect, such as bundle branch block or arborization block, (4) paroxysmal tachycardia (usually supraventricular) with 2:1 block, (5) atrial flutter with 4:1 block, (6) nodal rhythm, when the cardiac rate is not unduly slow, (7) complete AV block (rarely) with unusually high idioventricular rate (e g , congenital or diphtheritic), (8) sinus tachycardia, with alternating block (either SA or AV block).

Electrocardiography is usually essential for diagnosis of this group of cases

Type IV: Regular Rhythm with Unequal Force of Beats. (1) Pulsus alternans, (2) pulsus paradoxus, (3) regularly alternating extrasystoles.

Clinical diagnosis is usually possible on the basis of "spacing" of the beats.

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stance, in *sinus rhythm,* normal a, c, and v waves are seen, together with a characteristic systolic collapse of the jugular vein synchronous with each heart beat. On the other hand, in *nodal rhythm,* there is a large systolic pulsation or wave with each beat, because of simultaneous contraction of the right atrium and ventricle. In the *first-degree AV block,* with increased P-R interval, a characteristic delay occurs between the a and the c-v waves of the venous pulse; in *partial heart block,* a number of a waves are visible between the other waves and the degree of block can be determined by counting the ratio of a waves to radial pulses. In *complete heart block,* besides the phenomena of extra a waves, there are occasional large venous pulsations (familiarly known as "cannon waves"), owing to simultaneous contraction of atria and ventricles. In atrial fibrillation, even with slow rates, the absence of a waves reveals the diagnosis. In *atrial flutter,* typical, rapid, regular waves are visible during the diastolic pauses. Multiple and frequent *extrasystoles* can be differentiated from atrial fibrillation because the systolic collapse of the vein that occurs in the latter tends to decrease or disappear in the former.

Examination of the Heart. Sinus bradycardia, sinus arrhythmia, and *sinus tachycardia* are either physiologic or they are manifestations of cardiac or systemic disease *Premature contractions* and *paroxysmal supraventricular tachycardia* are more often associated with normal hearts than with diseased ones Diseases of the gastrointestinal and biliary tracts may induce reflex extrasystoles. *Paroxysmal ventricular tachycardia* seldom occurs except with severely damaged hearts *Atrial fibrillation* may be connected with mitral stenosis, coronary sclerosis, or hyperthyroidism, in the latter case, fibrillation tends to be paroxysmal In rheumatic fever, first-degree heart block is common and is of diagnostic significance. Diphtheria may cause a varying degree of AV block. Atrial flutter and heart block may be associated with congenital heart disease. A high systolic and a low diastolic pressure is usual in complete heart block

CHARACTER OF APEX BEAT. Palpation of the cardiac apex may suggest the existence of bundle branch block in the event of a bifid or double thrust, and of pulsus alternans in the event of alternately vigorous and feeble pulsations. Detection of a displaced apex beat or thrill at the apex may indirectly suggest the nature of the arrhythmia, by disclosing the presence or nature of organic heart disease.

HEART SOUNDS. The nature of an arrhythmia may be suggested by careful auscultation of the heart sounds, particularly at the apex. In *nodal rhythm,* the 1st sound tends to become louder each time that the atria and ventricle contract simultaneously. While in *paroxysmal atrial tachycardia,* the intensity of the 1st sound is constant from beat to beat, in *ventricular tachycardia* it may show a characteristic variation. In *atrial fibrillation and flutter* (particularly in the latter), the 1st sound tends to vary in intensity; in atrial fibrillation, the 2d sound may be absent, whenever the ventricular contraction fails to open the semilunar valves In *atrial flutter,* extra sounds, due to audible atrial contractions, may be heard during diastole. In *first-degree AV block,* either the 1st sound becomes attenuated in intensity or an extra sound is heard in diastole because of early atrial contraction. In *second-degree AV block,* the 1st sound may be preceded by an atrial sound, a phenomenon never observed in SA block. In *complete AV block,* there is a slow but regular ventricular rate of 20 to 40 beats per minute, with variations in intensity of the 1st sound, which assumes at times a loud and explosive character, commonly referred to as *bruit de cannon.* Splitting of the 1st and 2d sounds may occur in *bundle branch block;* a diastolic triple rhythm in conjunction with *pulsus alternans* may also suggest this condition.

Special Methods of Clinical Examination. EFFECT OF EXERCISE. Acceleration of the pulse after exercise, atropine, or amyl nitrite, by its action on the cardiac arrhythmia, may supply information of diagnostic value. Although exercise tends to increase the cardiac rate in sinus tachycardia, it has no effect on the rate of paroxysmal tachycardia The irregularity of the pulse in atrial fibrillation is usually accentuated by exercise. Exercise has little or no effect on the ventricular rate of complete heart block, but may cause the ventricular rhythm of the Wenckebach type of AV block to return to normal In atrial flutter, the ventricular rate may be suddenly doubled by exercise, in sinus rhythms, the rise of rate tends to be gradual.

EFFECT OF RESPIRATION. Sustained and deep respiratory effort, whether inspiratory or expiratory, may terminate an attack of supraventricular tachycardia by stimulating the vagus nerve. The simple maneuver of holding the

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Type V: Irregular Rhythm with Slow Rate (Arrhythmic Bradycardia). (1) *Sinus arrhythmia with sinus bradycardia,* (2) *sinus* bradycardia with *sinus* pauses or SA block, (3) sinus bradycardia with extrasystoles (atrial, nodal, or ventricular), (4) nodal arrhythmia, (5) incomplete AV block with frequent dropped beats, (6) unstable AV block, (7) atrial flutter, with variable and *high degree* of block, (8) atrial fibrillation *with slow ventricular* response.

In the majority of cases, a clinical diagnosis is possible through careful interrogation and examination of the patient.

Type VI: Irregular *Rhythms with Rapid* Rate (Arrhythmic Tachycardia). (1) *Atrial fibrillation,* (2) atrial flutter, (3) sinus *tachycardia with multiple extrasystoles,* (4) *AV* dissociation (interference dissociation), (5) *paroxysmal* ventricular tachycardia

Clinical diagnosis is *usually* facilitated by (*a*) *artificially* raising the cardiac rate with exercise, atropine, or amyl nitrite, (*b*) careful palpation of the pulse, for timing of beats, "pulse deficit," and "dominant rhythm"; (*c*) study of the 1st sound for variations in intensity.

Type VII. Irregular Rhythm with Normal Rate. (1) *Sinus arrhythmia,* (2) normal sinus rhythm *with extrasystoles (atrial,* nodal, or ventricular), (3) *SA* block, (4) sinus pauses, (5) partial AV *block* with irregular dropping of beats, (6) Wenckebach type of AV block, (7) interference dissociation.

Clinical diagnosis is usually possible after a *careful interrogation* and examination of the patient.

Type VIII. Clinically Silent (Imperceptible) *Rhythms.* This group of arrhythmias is characterized by the complete absence, clinically, of all pulsatory phenomena, arterial, venous, and cardiac (1) *severe tachycardia* (e g, 1:1 atrial flutter), (2) *ventricular flutter,* (3) ventricular fibrillation, (4) paroxysmal tachycardia with ineffective systolic contractions (rare), (5) severe shock (e g, after coronary thrombosis), (6) long sinus pauses or cardiac standstill (e g, AV block with Stokes-Adams syndrome).

A careful study of symptoms and signs may furnish the required information, otherwise, an electrocardiogram is indicated for diagnosis.

CONCLUSION

Despite the apparent complexity of cardiac arrhythmias, careful history taking, physical examination, and simple methods of clinical investigation often make it possible to recognize the nature of cardiac arrhythmias without having recourse to specialized methods of instrumental investigation, such as electrocardiography.

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into a bridging leaflet, or such bridging may occur between a cleft portion of the medial tricuspid and the anterior portion of the anterior mitral leaflet There is always a combined septal defect consisting of a patent foramen primum and a ventricular septal defect The size of this defect varies markedly. The right atrium and ventricle are hypertrophied, and the pulmonary artery is large. The left side of the heart varies in size

PATHOGENESIS OF THE COMPLEX. The pathogenesis of the common AV orifice and the combined defect has been discussed in Chap 1. The right atrium and ventricle present a volume and pressure hypertrophy. There is increased pulmonary flow. The size of the left ventricle varies according to the size of the atrial and ventricular septal defects, the amount of pulmonary flow, and the competence of the left side of the common valve

Complexes Associated with Anomalous Pulmonary Venous Drainage. The usual method of such drainage is by way of the coronary sinus, the left innominate, or a persistent left superior vena cava (Brody, Gott et al.). Uncommonly, the pulmonary veins drain directly into the right atrium Less frequently, they may enter the right superior vena cava, the inferior vena cava, the portal vein, a pancreatic vein, or the ductus venosus One, two, or all pulmonary veins may thus drain into the systemic venous circuit. Such drainage is associated with one of the two following complexes

PARTIAL ANOMALOUS PULMONARY VENOUS DRAINAGE In this complex, either the right or the left pulmonary veins drain into the systemic veins or into the right atrium. Frequently, there is an associated atrial septal defect. The right atrium and ventricle are hypertrophied, and the pulmonary artery is dilated, while the left side is normal. There may be an associated pulmonary or mitral stenosis.

TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE In this complex, all four pulmonary veins enter the systemic venous circuit (Fig. 6-13B, C) There is always a patent foramen ovale, and there is marked hypertrophy of the right atrium and ventricle. The pulmonary artery is large. The left side of the heart and aorta are small

PATHOGENESIS OF THE COMPLEX The embryogenesis of the pulmonary veins has been described (see Chap. 1). The right atrium and ventricle present a volume hypertrophy, and the left atrium and ventricle a volume atrophy.

Complexes Associated with Congenital Pulmonary Stenosis and Normal Aortic Root. In this complex (Campbell, 1954, Engle and Taussig), the pulmonary stenosis is usually valvular (Fig 6-13D). The pulmonic valve

Fig 6-12. Ventricular septal defect. A Left ventricular view. B, Right ventricular view.

is converted into a ringlike structure with a small opening, or less commonly, there is irregular thickening and adhesion between the cusps, producing a narrowing. The aorta arises in a normal position, and the architecture of the right ventricle is normal. The *crista supraventricularis* is hypertrophied but normal in architecture. There may be mild narrowing of the conus, or sometimes the primary stenosis is at the lower conal orifice. There is marked right ventricular hypertrophy and, in the later stage of the process, left atrial and left ventricular hypoplasia. The pulmonary stenosis may be isolated or associated with an atrial or, less commonly, a ventricular septal defect.

PATHOGENESIS OF THE COMPLEX. The right ventricle presents a pressure hypertrophy. The size of the left side is normal, at an early stage, when there is normal pulmonary flow. In the later stages, with the onset of failure, pulmonary flow is diminished, hence the smallness of the left side.

Complexes Associated with Isolated Congenital Supraaortic, Aortic, and Subaortic Stenosis (Lev, 1954, Campbell and Kauntze; Mencarelli). The aortic outflow tract may be



Fig. 6-13. A. Common AV orifice. Right atrial and right ventricular view. Arrow points to the combined defect. B. Heart returned to position, showing entry of left superior vena cava into the innominate. In (B) and (C) C, confluence of pulmonary veins, L, left superior vena cava; I, innominate; R, right superior vena cava. C. Total pulmonary venous drainage into a partial left superior vena cava, which in turn drains into the innominate vein. Heart lifted upward to show the confluence of the pulmonary veins draining into the left superior vena cava. D. Isolated pulmonary stenosis. Right ventricular view. Arrow points to the stenosis. (From M. Lev. *Autopsy Diagnosis of Congenitally Malformed Hearts.* Charles C Thomas, 1953.)

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narrowed below the aortic orifice, at the aortic orifice, or at the upper margins of the sinuses of Valsalva (Fig 6-14A). In *subaortic stenosis*, there is a thickened ridge of endocardium and sometimes myocardium extending across the base of the ventricular septum, beneath the pars membranacea, up to and involving the aortic leaflet of the mitral valve This usually produces a mild or moderate stenosis. In *aortic stenosis*, there is either a contraction of the aortic ring or a congenital deformity of the aortic valve with narrowing of the orifice This valve may be *bicuspid*, with deformity of the cusps, or the entire valve may produce *a ring*, with no distinct division into cusps In *supravalvular aortic stenosis*, there is a contraction of the aorta at the upper margins of the sinuses of Valsalva In all these complexes, there is left ventricular hypertrophy In subaortic stenosis, there may be an associated bicuspid aortic valve and an *aneurysm of a sinus of Valsalva*.

Complexes Associated with Isolated Aberrant Origin of a Coronary Artery from the Pulmonary Artery. Either the left or the right coronary artery (Bland et al.; Gasul and Loeffler) may have an abnormal origin from the pulmonary artery (Fig 6-14C) It is not known whether both may originate from this vessel Two different complexes therefore result

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subendocardial fibrosis Calcification of the myocardium may occur, and occasionally an infarct of the myocardium may be present.

RIGHT CORONARY FROM THE PULMONARY. There are no remarkable changes in the myocardium until adult life, when the patient may develop right ventricular failure.

PATHOGENESIS OF THE COMPLEX When the left coronary artery originates from the pulmonary, there are ischemic hypertrophy and degenerative changes of the left ventricle The effects upon the myocardium are related to the supply to the myocardium of blood with low oxygen content and under low pressure When the right coronary artery originates from the pulmonary, there are lesser changes in the right ventricle, possibly related to a greater supply of blood through the thebesian circulation on the right side

Complexes Associated with Congenital Aneurysm of an Aortic Sinus of Valsalva. Such aneurysms involve the right sinus of Valsalva



Fig 6-14 A. Supravalvular aortic stenosis Left ventricular view B Aneurysm of an aortic sinus of Valsalva. Arrow points to the aneurysm. C. Aberrant origin of left coronary artery from the pulmonary artery. Arrow points to the left coronary artery (From M. Lev. Autopsy Diagnosis of Congenitally Malformed Hearts Charles C Thomas, 1953)

(Feldman et al.; Goehring) most frequently, less frequently the left or posterior sinuses, and rarely all sinuses (Fig. 6-14C). These may point toward or rupture into the right atrium, right ventricle, left atrium, left ventricle, pericardial sac, mediastinum, pulmonary artery, inferior vena cava, or left pleural cavity. Such an aneurysm may secondarily produce aortic insufficiency, tricuspid stenosis or insufficiency, conduction defects, or myocardial infarction secondary to compression of a coronary artery.

Esophageal, Tracheal, and Bronchial Dislocation or Compression by Vessels. Such dislocation or compression (Edwards, 1948; Ellis et al., 1955) most commonly is produced by (1) a double aortic arch (Fig 6-15A), (2) origin of the right subclavian from the descending aorta, (3) a right aortic arch with a left descending aorta pulled over by a ductus arteriosus or a left subclavian Rarely an anomalous left pulmonary artery may compress the right main bronchus.

Complex Associated with Isolated Aortopulmonary Septal Defect. An aortopulmonary septal defect (Downing; Kirklin et al., 1955) is a round or oval opening between the aorta and the pulmonary artery, situated usually just above the aortic valve (Fig. 6-15B). This leads to right ventricular hypertrophy, but both ventricles may be hypertrophied. The pulmonary artery is dilated, and secondary changes may occur at the pulmonic valve. The anomaly may be associated with a patent ductus arteriosus, patent foramen ovale, ventricular septal defect, or bicuspid aortic valve.

PATHOGENESIS OF THE COMPLEX The right ventricle presents a pressure hypertrophy due to pulmonary hypertension. The left ventricle may show a volume hypertrophy

Idiopathic Hypertrophy of the Heart with Fibroelastosis. Here the entire heart is hypertrophied, or only the left ventricle. There is *fibroelastosis* (Weinberg and Himmelfarb, Johnson, 1952) of the left ventricle with or without involvement of the aortic and mitral valves. The left atrium and right ventricle may show similar changes The cause of the hypertrophy is not apparent, unless it is the fibroelastosis.

Bicuspid Aortic Valve. A bicuspid aortic valve (Abbott, 1932; Gross, 1937) consists of either two distinct cusps or a distinct cusp and an undivided double cusp (Fig 6-15C). The latter presents itself as a single cusp with low raphé dividing. Usually the right and left are represented in the double cusp, less frequently the right and posterior, and least frequently the left and posterior.

A bicuspid aortic valve may be associated with no pathologic complex It may, however, be associated with secondary hemodynamic or inflammatory change to produce an *aortic stenosis.*

Cor Biatriatum Triloculare, Cor Biloculare without Transposition, and Cor Triatriatum. In *cor biatriatum triloculare,* only a vestige of the ventricular septum is present. The atrial septum and the mitral and tricuspid orifices are well formed. This condition may be associated with complete transposition as described above, or it may be present without it. In *cor biloculare,* only remnants of the atrial and ventricular septa are present, producing in effect a common AV orifice (Conn et al.; McLester et al).

There are various forms of *cor triatriatum* (Pederson and Therkelson). In one form (*double left atrium*), a septum stretches across the left atrium, separating the opening of the pulmonary veins from the mitral orifice. There are thus two left atrial chambers, the right posterosuperior chamber receiving the pulmonary veins and the left anteroinferior chamber bearing the auricular appendage and communicating with the mitral orifice. The septum separating them usually has a defect. Where this septum is complete, the only exit from the pulmonary vein chamber is a channel draining wholly into the superior vena cava. With this anomaly, there is right atrial and right ventricular hypertrophy, dilated pulmonary artery, and small left ventricle The dynamics here are similar to those of mitral stenosis.

In a second type of cor triatriatum, the pulmonary veins enter the left, the superior vena cava the middle, and the inferior vena cava the right atrium In a third variation, the pulmonary veins enter the left and the normal superior and inferior venae cavae the right. A third chamber lies between the septum primum and secundum receiving the left superior vena cava, entering the coronary sinus

Dextrocardial Complexes. In *dextrocardia* and *dextroversion* (Lev, 1953, Lichtman), the apex-base axis points toward the right and downward (Fig 6-16) In dextroversion, this

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is due to extraneous pathologic changes shifting or rotating the heart. In dextrocardia, the position is due to inherent structure of the heart itself. There are three types of dextrocardia, depending upon the position of chambers. (1) *mirror-image dextrocardia*, (2) *pivotal dextrocardia*, and (3) *mixed dextrocardia*. In mirror-image dextrocardia, the morphologically left *atrium* and ventricle are situated posteriorly and to the right, while the morphologically *right* atrium and ventricle are situated *anteriorly* and to the left. This type of dextrocardia may be associated with generalized *situs inversus*, or it may be isolated.



Fig 6-15 A Double aortic arch. *A*, ascending aorta; *L*, left aortic arch; *R*, right aortic arch, *D*, descending aorta, *T*, trachea, *E*, esophagus. B Aortopulmonary septal defect. Small white rod passes through the defect. C. Bicuspid aortic valve. (B, C From M. Lev. Autopsy Diagnosis of Congenitally Malformed Hearts. Charles C Thomas, 1953.)

When it is the former, there is usually no congenital heart disease. In the latter, a true congenital heart disease exists, with all the complexes seen in levocardia being found in dextrocardia. In pivotal dextrocardia, the position of chambers is such as would be obtained if the heart in pure levocardia were rotated anteriorly and to the right in a horizontal plane. Thus, the morphologically left atrium and ventricle are situated anteriorly and to the left, while the morphologically right atrium and ventricle are situated posteriorly and to the right. This type of dextrocardia is always found in the isolated form, and most cases of isolated dextrocardia are of this type. They are always associated with congenital heart disease, and all types of such disease found in levocardia may be found here. In mixed dextrocardia, the atria and ventricles do not correspond Thus the atria may be in pivotal position and the ventricles in mirror image, or vice versa. Again any type of complex malformation may accompany this arrangement of chambers.

The combination of dextrocardia, hypertrophic rhinitis, nasal polyposis, sinusitis, and bronchiectasis is called *Kartagener's disease*

Isolated Levocardia. The apex-base axis of the normal heart points to the left and down and may be said to be in a state of levocardia. When this position is obtained in association with transposition of the abdominal viscera (Campbell and Forgacs), there is an isolated levocardia. There are two basic complexes associated with this position. In one, the superior vena cava is on the left side and the heart chambers are transposed, with a right aortic arch. Some form of transposition of the arterial trunks, ventricular septal defects, and pulmonary stenosis are often associated. In the second type, the superior vena cava is on the right side and the chambers are in normal position. Here, there is defective septation of atria and ventricles, with transposition of the arteries and abnormalities in systemic and sometimes venous return.

Mixed Levocardia. In this condition (Lev, 1953) the base-apex axis points toward the left and down, but the atria and ventricles do not correspond (Fig. 6-17A). Sometimes the atria and sometimes the ventricles are transposed. This position of the chambers may be associated with any type of congenital heart disease.

Rare Complexes. In *congenital idiopathic dilatation of the pulmonary artery,* the pulmonary artery is large, the aorta small, and the right ventricle may or may not be hypertrophied The right ventricular pressure is normal, but there is a drop in pressure in the pulmonary artery In *isolated congenital mitral stenosis,* a deformed mitral valve is present without any deformity of the aortic valve Rarely there is *combined stenosis of the aortic and pulmonic valves* In *congenital tricuspid insufficiency,* the valve may consist of two

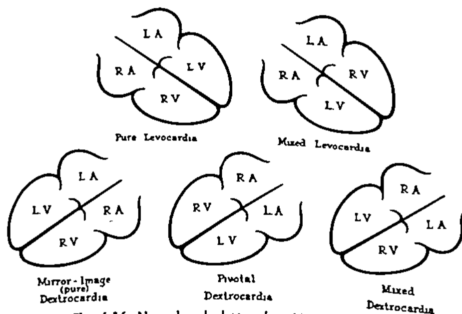


Fig. 6-16. Normal and abnormal position of chambers

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leaflets, an anterior and a fused posteroseptal, both attached to the septal wall by short slender chordae, or the chordae may be connected to small rudimentary papillary muscles In *premature closure of the foramen ovale,* this opening is closed at birth. There is an associated small left atrium and ventricle and enlarged right side

Complexes Associated with Other Diseases. In *Marfan's syndrome* (McKusick), the most common associated cardiac complex is aneurysmal dilatation of the ascending aorta, aneurysms of the sinuses of Valsalva, dilatation of the aortic ring with regurgitation, and upward displacement of the coronary ostia Another common complex is mild coarctation of the aorta, dilatation of the ascending aorta, aneurysms of the sinuses of Valsalva, with or without a left superior vena cava Both complexes may end in dissecting aneurysm. In some cases, there is idiopathic dilatation of the pulmonary artery, an atrial septal defect, a patent ductus arteriosus, a tetralogy of Fallot, congenital mitral insufficiency, pectus excavatum, kyphoscoliosis, or conduction disturbances In *pectus excavatum,* the heart is displaced to the left and upward and is flattened in the anterior and the posterior diameters

In *gargoylism* (*lipochondrodystrophy*) (Emanuel), there is thickening and nodularity of the mitral, aortic, tricuspid, and pulmonic valves in order of occurrence, associated with thickening of the ventricular endocardium and chordae. The right atrium and ventricle are hypertrophied, and the pulmonary artery is large.

Malignant carcinoids (Branwood et al.) may be associated with fibrosis and thickening of the endocardium of the right ventricle with involvement of the pulmonary or the tricuspid valves, or both, with resultant pulmonary stenosis, with or without tricuspid stenosis or insufficiency.

Agenesis of the spleen (Ivemark) is associated with common AV orifice, persistent ostium primum, pulmonary stenosis or atresia, dextrocardia, transposition complexes, anomalous pulmonary venous drainage, and right aortic arch In *glycogen storage disease,* the heart may be diffusely hypertrophied, with glycogen infiltration of the sarcoplasm of the myocardial fibers







Fig 6-17. A Mixed levocardia. Right atrial and left ventricular view C, coronary sinus, I, inferior vena cava B. Rete Chiari C Double mitral orifice Arrow points to accessory mitral orifice (B From M Lev, *Autopsy Diagnosis of Congenitally Malformed Hearts* Charles C Thomas, 1953)

When it is the former, there is usually no congenital heart disease. In the latter, a true congenital heart disease exists, with all the complexes seen in levocardia being found in dextrocardia. In pivotal dextrocardia, the position of chambers is such as would be obtained if the heart in pure levocardia were rotated anteriorly and to the right in a horizontal plane. Thus, the morphologically left atrium and ventricle are situated anteriorly and to the left, while the morphologically right atrium and ventricle are situated posteriorly and to the right This type of dextrocardia is always found in the isolated form, and most cases of isolated dextrocardia are of this type They are always associated with congenital heart disease, and all types of such disease found in levocardia may be found here In mixed dextrocardia, the atria and ventricles do not correspond. Thus the atria may be in pivotal position and the ventricles in mirror image, or vice versa Again any type of complex malformation may accompany this arrangement of chambers

The combination of dextrocardia, hypertrophic rhinitis, nasal polyposis, sinusitis, and bronchiectasis is called *Kartagener's disease*

Isolated Levocardia. The apex-base axis of the normal heart points to the left and down and may be said to be in a state of levocardia. When this position is obtained in association with transposition of the abdominal viscera (Campbell and Forgacs), there is an isolated levocardia. There are two basic complexes associated with this position. In one, the superior vena cava is on the left side and the heart chambers are transposed, with a right aortic arch. Some form of transposition of the arterial trunks, ventricular septal defects, and pulmonary stenosis are often associated In the second type, the superior vena cava is on the right side and the chambers are in normal position. Here, there is defective septation of atria and ventricles, with transposition of the arteries and abnormalities in systemic and sometimes venous return.

Mixed Levocardia. In this condition (Lev, 1953) the base-apex axis points toward the left and down, but the atria and ventricles do not correspond (Fig. 6-17A). Sometimes the atria and sometimes the ventricles are transposed. This position of the chambers may be associated with any type of congenital heart disease.

Rare Complexes. In *congenital idiopathic dilatation of the pulmonary artery,* the pulmonary artery is large, the aorta small, and the right ventricle may or may not be hypertrophied The right ventricular pressure is normal, but there is a drop in pressure in the pulmonary artery. In *isolated congenital mitral stenosis,* a deformed mitral valve is present without any deformity of the aortic valve. Rarely there is *combined stenosis of the aortic and pulmonic valves.* In *congenital tricuspid insufficiency,* the valve may consist of two

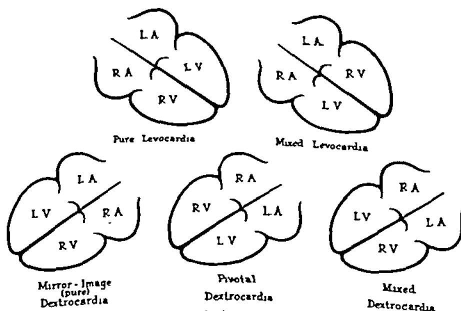


Fig. 6-16. Normal and abnormal position of chambers.

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ond valvular opening supplied with its own leaflets, chordae, and papillary muscles, lying within the segments of an otherwise normal orifice, or there may be two orifices lying side by side of equal or unequal thickness. In double mitral orifice (Fig 6-17C), the accessory (usually smaller) orifice may lie in the anterior or inferior mitral leaflet, having two leaflets of its own joined to the anterior or inferior papillary muscles In some cases, each orifice has one leaflet, with the two orifices joined by a fibrous tissue ridge

BICUSPID AND IRREGULARLY FORMED PULMONIC VALVE. This valve may consist of two well-approximated cusps, or the cusps may be small and insufficient. At times, a portion of the wall may be uncovered by cusp tissue This is usually associated with transposition or tricuspid atresia complexes Rarely it may be an isolated anomaly

ACCESSORY PULMONARY ARTERIES Such arteries may arise from the thoracic or abdominal aorta or from the seventh intercostal artery They may supply accessory lobes of the lung or the normal lung

CONGENITAL ANEURYSM OF THE PULMONARY ARTERY This usually involves the main trunk alone, but the entire secondary branches may also be involved It may be related to Marfan's syndrome or abnormally formed pulmonic valves

ABSENT DUCTUS ARTERIOSUS If the pulmonary arterial trunk and the two pulmonary arteries fail to develop, then the ductus arteriosus is also absent

BILATERAL DUCTUS ARTERIOSUS These may be connected to both the right and left pulmonary arteries, where there are complex malformations of the aortic arches.

ANEURYSM OF THE DUCTUS ARTERIOSUS This is a rare entity

ABNORMAL CHORDAE Chordae, bands, or reticula may be found in any chamber.

CONGENITAL DIVERTICULUM OF THE LEFT VENTRICLE. Here there is an outpouching of the heart lined by smooth, thickened endocardium, and whose wall consists of all three layers of the heart.

SUPERNUMERARY AND FENESTRATED SEMILUNAR CUSPS. The aortic and pulmonic valves may have four, five, or more cusps. Fenestrated cusps are commonly seen in the aortic valve and less commonly in the pulmonic valve. It is not known whether they are congenital.

ANOMALIES OF THE CORONARY ARTERIES ARISING FROM THE AORTA. There may be a single coronary artery arising from the aorta. This vessel may follow the course of the left or right coronary or neither, or it may divide into the normal left and right coronary arteries. Rarely, a coronary artery may supply the lung or anastomose with pulmonary branches. Rarely, a coronary artery may communicate with the right ventricle.

RIGHT AORTIC ARCH. There are two types of right aortic arch. (1) In one type, the aorta ascends toward the right, arches over the right bronchus, and descends over the right side of the vertebral column. The brachiocephalic vessels are given off in mirror image This is called simply *right aortic arch*. (2) In the second type, after arching over the right bronchus, the vessel deviates toward the left of the vertebral column, but still somewhat to the right of the position of the normal aorta. This is *right aortic arch with left descending aorta*. This is usually obtained by a *left-sided* ductus or left subclavian pulling the *right aortic arch* to the left.

OTHER ABNORMALITIES OF THE BRACHIOCEPHALIC VESSELS All the brachiocephalic vessels may arise as one from the aorta More commonly, the innominate and left common carotid may arise as one The left subclavian artery may originate from the aorta distal, at, or from the ductus arteriosus.

Congenital Glycogenic Tumors (Rhabdomyomas). These tumors (Lev) are most commonly found in the left ventricle. They may be single or multiple Generally, they are yellowish-white in color, homogeneous, and soft in consistency. Microscopically they consist of large vacuolated muscle cells containing glycogen. Associated with these tumors, there may be cysts or tumors of the kidneys, tumors of sebaceous glands, harelip, cleft palate, gliomas of the brain, and other congenital malformations of the pancreas, kidneys, and lungs.

Congenital Atrioventricular Block. This is associated with an interruptive lesion in the pre-AV nodal area, the AV node, or the bundle (Campbell and Thorne). Such lesions have been found in ventricular septal defect, patent foramen primum, and mixed levocardia and have been postulated in many other conditions.

Wolff-Parkinson-White Syndrome. This may be found in Ebstein's disease, ventricular septal defects, or coarctation of the aorta (Lev et al) This electrocardiographic abnormality may also be present without gross congenital malformations Aberrant muscular communications between the right atrium and right ventricle, the AV node and the ventricular musculature, or the left atrium and ventricle may be found in the syndrome

Incidental Malformations. In addition to the above malformations, which are best discussed as forming complexes, there are many other abnormalities which are incidental findings with little or no effect upon the heart (Lev, 1953, Abbott, 1927; Edwards, 1953)

DEFECTS OF THE PERICARDIUM These may be present on the anterior and left aspects of the heart, producing continuity between the pericardial sac and the left pleural cavity Occasionally, there is a localized defect in the region of the pulmonary artery The pericardium may be found unattached to the central tendon of the diaphragm The right pericardial wall may be attached to the chest wall

DIVERTICULUM OF THE PERICARDIUM. Such a formation may be found at the base of the aorta, or at the junction of the superior and inferior venae cavae on the right side, or at the junction of the pulmonary veins on the left side. This communicates with the main pericardial cavity by a small opening, which may close, producing a cyst.

ECTOPIA CORDIS. The heart may be displaced outside the thoracic cavity being (1) cervical, (2) thoracic with a fissure of the sternum, (3) abdominal with a defect of the diaphragm, or (4) thoracoabdominal. The myocardium may be completely exposed or covered by skin and subcutaneous tissue Ectopia cordis is usually associated with complex malformations of the heart and with skeletal abnormalities.

BIFID APEX. Here there are two apexes, one for the left and the other for the right ventricle. Where present alone, it is familial and hereditary.

DOUBLE AND LEFT CORONARY SINUS. Where the mouths of the coronary veins enter the left atrium, there is a blind sac for the entry of the coronary sinus into the right atrium The coronary veins may drain into two sinuses, each entering a single atrium.

PERSISTENT LEFT SUPERIOR VENA CAVA A left superior vena cava may be present together with a right superior vena cava, with or without a communication between them, or a left superior vena cava may be the sole venous brachiocephalic drainage. The latter usually enters the coronary sinus, less frequently the right atrium directly, the left atrium or both atria.

ABNORMAL RIGHT SUPERIOR VENA CAVA. This may enter the left atrium or it may straddle the atrial septum to enter both atria.

ABSENT INFERIOR VENA CAVA The upper part of the inferior vena cava is absent, the hepatic veins entering the heart directly. The azygos veins drain the lower extremities

RETE CHIARI This consists of a network of fine endocardial fibers, extending from the eustachian and thebesian valves to the linea terminalis (Fig 6-17B) This may be the seat of thrombosis

ABNORMAL EUSTACHIAN AND THEBESIAN VALVES. Either may be absent, enlarged, or fenestrated. They may be represented by a common valve

ANEURYSMAL DILATATION OF THE FOSSA OVALIS The atrial septum in the region of the fossa ovalis may be outpouched in either direction The limbus usually has a wide arc, and part of it may be included in the aneurysm

DOUBLE TRICUSPID AND MITRAL ORIFICES In double tricuspid orifice, there may be a sec-

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sis and significance of alterations of the pulmonary vascular bed were questioned Anatomic vascular alterations have been described in an ever-increasing number of diseases, both cardiac and pulmonary. These alterations may be primary, but more likely they result from the underlying cardiac or pulmonary disease; their presence, however, may significantly ef-

Anatomic Classification of Congenital Heart Disease

Group I Defects between great vessels or ventricles with or without pulmonary stenosis

- *A* Simple defects
  1. Patent ductus arteriosus
  2. Aortic septal defect
  3. Single ventricle
  4. Ventricular septal defect
  5. Truncus arteriosus
- *B* Complicated defects
  1. Ruptured sinus of Valsalva into right ventricle
  2. Coarctation of the aorta distal to a patent ductus
  3. Coarctation of the aorta proximal to a patent ductus
  4. Single ventricle with transposition of great vessels
  5. Atrioventricularis communis
  6. Biloculate heart
  7. Tricuspid atresia
  8. Tricuspid atresia with transposition
  9. Corrected transposition of great vessels with ventricular defect
  10. Transposition of the great vessels with
      - *a* Patent ductus arteriosus
      - *b* Ventricular defect
  11. Taussig-Bing syndrome
- *C* Complicated defects associated with conditions causing an elevated pulmonary venous pressure
  1. Aortic atresia with patent ductus arteriosus and small patent foramen ovale
  2. Aortic and mitral atresia with patent ductus arteriosus and small *patent foramen* ovale
  3. Mitral atresia with ventricular defect and small patent foramen ovale
  4. *Mitral* stenosis with closed foramen ovale and
      - *a* Patent ductus arteriosus
      - *b* Ventricular defect

Group II Defects between atria with or without pulmonary stenosis

- *A* Simple defects
  1. Secundum defect
- *B* Complicated defects
  1. Mitral stenosis with large atrial septal defect [illegible]
  2. [illegible]
  3. [illegible] with atrial septal defect

- 4 Ebstein's disease with patent foramen ovale
- *C* Complicated defects associated with mitral insufficiency
  1. Primum defect with cleft mitral valve
  2. Secundum defect with mitral insufficiency (e g , short chordae)
- *D.* Complicated defects associated with pulmonary venous obstruction
  1. Mitral stenosis with small patent foramen ovale

Group III Defects of pulmonary venous drainage

1. Partial return to right atrium with or without patent foramen ovale
2. Total anomalous venous return with patent foramen ovale
   - *a* [illegible]
   - *b*
   - *c*
   - *d* [illegible] to coronary sinus
3. Total anomalous and obstructed venous return to portal system with patent foramen *ovale*

Group IV. Lesions not associated *with a communication*

- *A* Left-sided lesions
  1. Coarctation of the aorta
  2. Aortic stenosis
  3. [illegible]
  4.
  5. [illegible] pulmonary artery
- *B* Left-sided lesions always associated *with elevated* pulmonary venous pressure
  1. Congenital mitral stenosis
  2. Triatriculare biventricularis
  3. *Ebstein's* disease of the mitral valve
  4. Congenital pulmonary venous obstruction
  5. Congenital mitral *insufficiency*
- *C* Right-sided lesions
  1. Primary pulmonary vascular disease (*primary pulmonary* hypertension)
  2. Coarctation of the pulmonary arteries
  3. Valvular pulmonary stenosis
  4. Pure infundibular pulmonary stenosis
  5. Tricuspid stenosis
  6. Ebstein's disease with closed foramen ovale

Clinical aspects of congenital heart disease

J. FRANCIS DAMMANN, JR.

INTRODUCTION

In the formative years of a new medical discipline, diagnosis and treatment tend to be oversimplified and the emphasis is placed upon the obvious manifestations of a disease process The boundaries are determined in this way, and an understanding and treatment of the classical syndrome evolves It is only later that appreciation emerges of the subtle distinctions that alone may separate one condition from another So it is with the field of congenital heart disease. Led by Dr Maude Abbott, a determined effort was made to subdivide cardiac malformations in a reasonable way by carefully analyzing the classical syndrome and correlating clinical findings with the exact anatomic abnormality That this approach was successful cannot be denied, for rapidly there followed specific therapy for certain malformations. However, this approach is limited because it is based primarily upon an analysis of the anatomic variations (see the accompanying classification). Abbott, recognizing that progressive changes could occur, developed a classification which took into account alterations in hemodynamics In her analysis of the group of patients with cyanosis tardive in which a reversal of shunt occurs, she implies that a sound classification of congenital heart disease must be based on physiology as well as anatomy.

In the present-day approach to congenital cardiovascular disease, the role of the systemic and pulmonary circulation has achieved greater recognition as a determining factor in the clinical manifestations of a particular malformation of the heart Classifications of congenital heart disease are now concerned more with physiology than with anatomy. We appreciate fully that congenital heart disease is not static, we realize that the full implications of the natural history of the disease must be understood It is only in this way that the optimal results from therapy can be obtained since it is necessary to know not only the exact anatomy, but the ideal time for surgical intervention

In this chapter, an attempt will be made to integrate the pulmonary circulation with a particular malformation and to point out the clinical signs and symptoms which result from changes in the pulmonary vascular bed Therefore, before discussing the individual defects, it would be well to consider in general terms those factors in the pulmonary circulation which alter the clinical picture produced by cardiac anomalies On this basis, a physiologic classification of congenital heart disease is presented (Table 6-1), and each malformation will be discussed within the framework of this classification.

The important role of the lungs in shaping the clinical course of patients with heart disease has only recently been recognized. Respiratory function was the first to be studied The importance of the pulmonary circulation received recognition only when the pathogene-

defect joining the two circulations, if the shunt is sufficiently large to utilize the total available vascular bed (Dexter et al., 1950).

The Volume of Blood Present within the Lungs. The total vascular bed may be reduced functionally but not anatomically by an increase in pulmonary blood volume, such as the shift of blood from the systemic to the pulmonary circulation following an acute cerebral accident (Sarnoff et al, 1952, 1953).

Obstruction to the Passage of Blood from the Lungs. When pulmonary venous obstruction is present, an increase in pulmonary artery pressure is necessary to maintain flow through the lungs (Yu et al)

Alterations in Vasomotor Tone. Finally, it is probable that alterations in pulmonary arterial vasomotor tone (Wood, 1952), and perhaps in pulmonary venous tone as well, may bring about a rise in pulmonary artery pressure and lead eventually to pulmonary arterial hypertrophy and intimal thickening

In contrast to the normal adult lung, the *fetal lung*[2] is a high-pressure, high-resistance vascular system Space occupied by the lungs is reduced, for the diaphragm is high and the chest cage is concave. The pulmonary vessels are surrounded by a liquid, not a gas medium, since the alveoli are filled with amniotic fluid The presence of fluid rather than air in the alveoli means that the pressure exerted externally on the pulmonary vessels is increased, and consequently a greater intra-arterial pressure is necessary to maintain blood flow In contrast to the normal adult lung, the number of functioning capillaries and the total available vascular bed are small. The small pulmonary arteries and arterioles of the fetal lung resemble systemic vessels The media of the small muscular arteries is thick, and the lumen size is small. That the resistance to blood flow through the lung of a fetus is high is attested to by the fact that 50 per cent or more of the right ventricular output bypasses the lungs through the ductus arteriosus into the descending aorta (Reynolds) In fact, the major portion of blood reaching the umbilical cord is contributed by the right ventricle through the ductus arteriosus Since alterations in pulmonary resistance directly affect the amount of blood passing through the ductus to the umbilical cord, it is clear that the pulmonary vascular bed plays a vital role in the total circulation during fetal life.

The most important change occurring at the time of birth[3] is a shift in dependence for oxygen from the placenta to the lungs. The first breath expands the lungs with air, which forces amniotic fluid from the bronchi out toward the periphery of the lung, where it is absorbed into the blood stream. The replacement of fluid in the alveoli by air reduces the extravascular pressure exerted upon the pulmonary vessels. Intravascular pressure becomes sufficient to force open new vascular channels. Hence, there is a decrease in pulmonary vascular resistance, which is brought about by the increase in the total capillary bed and the decrease in extravascular pressure and is enhanced by the increase in chest and lung size and the development of intermittent negative intrathoracic pressure. Pulmonary artery pressure falls, the right-to-left shunt through the ductus is obliterated, pulmonary blood flow is increased, and the additional blood returned to the left atrium increases pressure in this chamber and closes the valve of the foramen ovale In early neonatal life, functional closure of the patent ductus arteriosus and patent foramen ovale is followed by anatomic closure (Patten, 1930).

At birth, pulmonary blood flow, previously only a fraction of the cardiac output, increases two- to tenfold The available vascular bed, on the other hand, increases many times more. Thus, a change occurs in the ratio of pulmonary flow to available vascular bed. A sufficiently large low-resistance bed is available so that normal increases in pulmonary blood flow do not cause a rise in pulmonary artery pressure. A high pulmonary vasomotor tone is no longer essential to the regulation of pulmonary and placental blood flow. Vasomotor tone, therefore, decreases, and disuse atrophy of the small muscular pulmonary arteries results (Dammann; Ferencz). Thick-walled fetal vessels with a small lumen become thin-walled and obtain a wide lumen The shift in the structure of the vessels can be demonstrated in the early months of life by a study of the lumen-wall ratios obtained by dividing the lumen diameter by the thickness of the media and intima, respectively.

[2] The fetal circulation is discussed in Part 1, Chap. 2 *Editor*.

[3] See Part 1, Chap 2 *Editor*.

TABLE 6-1. PHYSIOLOGIC INTERPRETATION OF ANATOMIC CLASSIFICATION

Group I Signs and symptoms dependent upon volume of pulmonary blood flow Flow affected by position and size of defect, severity of resistance to right ventricular output, severity of pulmonary venous obstruction

Size of defect	Degree of resistance to RV output *	*Physiologic changes*							*Signs and symptoms unrelated to failure*			Cardiac failure
		Size of RV	Size of LV	Size of LA	ECG	Ratio ventricular pressure	Direction of shunt	Ratio pulmonic to systemic flow	Dyspnea	Cyanosis	Growth failure	
Large (in which defect, because of physiologic size, cannot limit volume of shunt)	Mild or absent	4+	4+	2+	R & LVH	RV = LV	L R	4+/1−	1+	0	4+	L R
	Moderate	±	±	±	RVH LVH	RV = LV	L R	N+/N+	0	±	0	0
	Severe	2+	N	N	RVH	RV = LV	R L	−2/N	4+	4+	2+	R
Medium (in which defect, because of physiologic size limits shunt unless pulmonary resistance is high)	Mild or absent	1+	2+	1+	LVH RVH	LV RV	L R	3+/1−	1+	0	3+	L R
	Moderate	1+	N	N	RVH LVH	LV RV	L R	1+/N	0	0	0	0
	Severe	4+			RVH	RV LV	R L	−2/N	4+	2+	2+	R
Small (in which defect, because of physiologic size limits volume shunt totally)	Mild or absent	N	±	N	LVH	LV RV	L R	2+/N	0	0	0	0
	Moderate	2+	N	N	RVH	LV RV	L R	1+/N	0	0	0	0
	Severe	4+	N	N	RVH	RV LV	R L	1−/N	4+	2+	1+	R

* Resistance due to either pulmonary stenosis or pulmonary vascular disease

fect the course of the disease An adequate understanding of pulmonary vascular anatomy and function is, therefore, essential to the correct evaluation of patients with heart disease

The *vascular bed of the normal adult lung* is a low-pressure low-resistance system with the capacity to handle right ventricular outputs of three times the normal resting value without significant elevation in pressure[1] Pulmonary arteries of all sizes are thin-walled and have a large lumen Unlike systemic arterioles, which possess a muscular media capable of greatly increasing resistance to blood flow, the pulmonary arterioles contain only a few muscle fibers and can offer little resistance to the flow of blood. Pulmonary blood pressure is normally low; however, the pressure may rise under certain abnormal conditions, and if the rise is acute and severe, the thin-walled vessels are stretched beyond their tolerance, rupture of the intima occurs, and arteritis of varying severity follows. The end result is a markedly thickened vessel with a small lumen, extensive intimal proliferation, medial hypertrophy, and fibrosis. If, on the other hand, the rise in pulmonary pressure is chronic and less severe, there results a gradual hypertrophy of the media of the small pulmonary arteries so that the capacity of the pulmonary arterial bed to withstand and alter pressure is increased.

[1] See Part 2, Chap 25, for Physiology of the Pulmonary Vessels *Editor.*

There are five factors which control vascular resistance and pulmonary pressure.

The Capacity of the Pulmonary Vascular Bed. Cournand and others have demonstrated a change in pressure-flow relationships following reduction of functioning lung mass. After a pneumonectomy, the volume of blood passing through the remaining lung is approximately doubled Pulmonary arterial pressure is normal at rest, but with exercise, the available pulmonary vascular bed is not sufficiently large to handle the increased cardiac output without a rise in pressure Frequent elevations of pressure lead to arterial hypertrophy and eventual intimal sclerosis which, in turn, cause an increase in resistance to blood flow. A similar picture develops when sufficient pulmonary tissue is destroyed by such diseases as tuberculosis, emphysema, pulmonary fibrosis, and in childhood, repeated attacks of pneumonitis and asthmatic bronchitis.

The Volume of Pulmonary Blood Flow. Elevation of pulmonary artery pressure may result from a left-to-right shunt occurring through a

with a right-to-left shunt Early onset of fatigue and growth failure are common in both.

Do symptoms suggest left heart failure? *Orthopnea* strongly suggests left heart failure However, it is not a common finding in early childhood In infancy and early childhood, pneumonia is frequently the presenting complaint Left heart failure should always be suspected when a child with pneumonia does not respond to antibiotic therapy.

In noncyanotic patients, *hemoptysis* usually indicates left heart failure or pulmonary venous obstruction with increased intracapillary pressure In cyanotic patients, hemoptysis usually occurs from the rupture of a collateral or bronchial vessel and does not indicate left heart failure.

Do the symptoms suggest right heart failure? *Edema of the extremities* is readily discovered in older children In infants, however, pitting edema is rare, hepatomegaly being the most frequent finding A history of sudden weight gain is suggestive of the accumulation of edema fluid Occasionally the history of a decreased urinary output may be obtained

PHYSICAL EXAMINATION

Is the patient well developed and well nourished? Are cyanosis and clubbing present? Is the distribution uniform or unequal? Failure of development is more common when a cardiac malformation is severe. However, as a differential diagnostic point, failure of development is of no value. The *gracile habitus*, associated in the early literature with an atrial defect, is equally common with all defects (Abbott, 1927, Brown)

The *cyanosis* of congenital heart disease is usually *general*, involving primarily the lips and nail beds If it is *confined to the lower extremities and left hand*, this finding is pathognomonic of a large patent ductus with reversal of blood flow.

What is the character of the peripheral pulses? Carotid, radial, and femoral pulses should be evaluated both for their presence and for their comparative quality The diagnosis of coarctation of the aorta (particularly in infancy) may rest upon the difference in quality of radial and femoral pulses A *dampened femoral pulse*, but active radial pulse, suggests coarctation of the aorta A *bounding pulse* suggests aortic insufficiency or a communication between the aorta and pulmonary artery. A *weak pulse*, which is difficult to feel, is often present with congestive heart failure. However, it may indicate a decreased systemic flow and the presence of a large left-to-right shunt or obstruction in the outflow tract of the left ventricle.

Particularly in infancy, the feel of the pulse is a more reliable measure of blood pressure than the auscultatory method. A reliable blood pressure reading is difficult to obtain since the size of the cuff used, the thickness of the arm and thigh, and the activity of the infant all cause marked variations.

Is edema present? Pitting edema is easily discovered. In early infancy, however, edema does not pit and may be missed. If the skin is thick, pasty, and varies in quality from the extremities to the trunk, it is good evidence that edema is present The skin of babies with severe forms of congenital heart disease not leading to cardiac decompensation is characteristically loose, easily picked up, and lacking in tone.

Specific Cardiac Examination. Is there a bulge of the left chest? Because of the position of the right ventricle close to the chest wall, *a bulge of the left chest* indicates enlargement of the *right* ventricle. Such a bulge is not seen with left ventricular enlargement alone

Is precordial activity increased or decreased? Increased activity of the precordium, close to *the sternum*, suggests a large right ventricle and a high pulmonary artery flow. A comparison of the activity close to the sternum and at the apex *should* be made, for when the left ventricle does *not* have an increased work load and the *right does*, apical pulsations are less than those close to the sternum. Decreased precordial *activity* suggests stenosis or pulmonary vascular disease. On the other hand, a swing of the chest from left to right with each beat of the heart develops from tricuspid or mitral insufficiency.

What is the position of the apex? In infants and children the *apex* normally can be *felt in the 4th left* interspace When it is felt in the 5th left interspace, the probability of left ventricular enlargement must be entertained. If the apex is felt lateral to the midclavicular

The factors controlling pulmonary blood pressure have been previously mentioned. If any one of them is sufficiently altered at birth, the fetal pulmonary vascular pattern will persist (thick-walled pulmonary vessels with a small lumen), and pulmonary hypertension will continue. If an alteration in any factor occurs after disuse atrophy of the small pulmonary vessels has taken place, medial hypertrophy must be reacquired and the likelihood of significant vascular injury is greatly increased. As a consequence, *the picture of pulmonary hypertension in malformations active at birth is one of marked medial hypertrophy with little intimal change,* whereas *medial hypertrophy is less extensive and intimal proliferation and scarring are more common when pulmonary hypertension occurs at a later date*

The importance of pulmonary hypertension in congenital heart disease is obvious. Of equal importance to the presence of pulmonary hypertension, however, is the method by which that hypertension was brought about, the time it occurred, and the specific response of the pulmonary vascular bed to it (Dammann, 1958) It is only with a full understanding of these factors that proper selection of patients for cardiac surgery can be made. For example, patients with an atrial septal defect who develop pulmonary vascular disease, right heart failure, and a reversal of shunt are poor candidates for closure of the defect because the pulmonary vascular disease is in good part irreversible, consisting primarily of marked intimal thickening On the other hand, the patient with a large patent ductus and pulmonary hypertension, where the shunt is predominantly left to right, can be greatly assisted by closure of the ductus, for medial hypertrophy of the small pulmonary vessels is the predominant morphologic change and such hypertrophy is reversible once the stimulating mechanism is removed.

The accurate diagnosis of congenital heart disease depends upon the correct interpretation of all available data Adequate data can be obtained and properly assessed if a routine plan of investigation is adhered to. The basic approach is to isolate that portion of the circulatory system which is under stress, to determine when stress first appeared, and to assess its magnitude The answers to these questions should be obtained.

HISTORY [4]

At what age did symptoms appear? Have they increased, remained stationary, or decreased in severity? We have found it very useful to obtain a detailed developmental history. It is common for patients with a ventricular septal defect, for example, to appear normal at birth, show poor weight gain, rapid respiration, and susceptibility to pulmonary infections for the first year or two and then to improve The improvement may be sufficient to make both doctor and parent assume that the defect is no longer important. This period of well being—the "golden period"—is temporary, however, and leads to a gradual downhill course characterized by increasing cyanosis and decreasing exercise tolerance. In contrast, patients with an atrial septal defect usually do well in the first years of life, and the appearance and progression of symptoms is relatively late and slow.

When was the murmur first heard? If a systolic murmur was heard in the newborn period, the diagnosis of valvular or subvalvular stenosis or a small ventricular septal defect is suggested A murmur is rarely heard in the newborn infant due to a patent ductus arteriosus, a transposition of the great vessels, a large ventricular defect, or an atrial defect.

Do the symptoms suggest a right-to-left shunt? Cyanosis suggests a right-to-left shunt although the cyanosis of venous stasis secondary to right heart failure and deficient oxygenation from other causes must be ruled out. The cyanosis of congenital heart disease involves primarily the lips and nail beds. Unless parents are questioned carefully, the examiner may be misled, for many normal children have transient cyanosis around the mouth, but not of the lips alone. The history of *transient cyanosis* in the newborn period is not uncommon in patients with septal defects or isolated valvular pulmonary stenosis.

Do symptoms suggest a left-to-right shunt? Repeated pulmonary infections are far more commonly seen when a left-to-right shunt is present than when the shunt is right to left. *Exertional dyspnea* is usually less severe than

[4] The history and physical examination in children have been discussed in Part 3, Chap. 10. *Editor.*

line in the 4th left interspace, it suggests right ventricular enlargement alone.

Auscultatory Findings. Much information can be obtained from a proper evaluation of *murmurs.* The point of maximal intensity, distribution over the precordium, distribution to the axillae and to the great vessels of the neck, timing, duration, and quality of the murmur all are important

POINT OF MAXIMUM INTENSITY In general, a *systolic murmur,* maximal at the base of the heart in the 2d and 3d interspace, suggests relative or absolute *obstruction* of the pulmonic or aortic orifices, ventricular defect, or tricuspid insufficiency. A systolic murmur maximal at the apex suggests mitral or occasionally tricuspid insufficiency

DISTRIBUTION. Certain congenital malformations of the heart are characterized by a distinctive distribution of the murmur For example, the murmur of isolated valvular pulmonary stenosis is maximal in the 2d left interspace, is very well transmitted up toward the left clavicle, and is frequently associated with a *thrill* over the left clavicle. In older children, the murmur of aortic or subaortic stenosis is heard best to the right of the sternum in the 1st and 2d right interspace and is well transmitted along the great vessels to the neck In infants, however, it may be heard best low over the sternum to the left of the midline

It is important to evaluate the distribution of the murmur carefully. The stethoscope should be moved from the point of maximal intensity in all directions to determine where the murmur is best transmitted. Not infrequently, a systolic murmur may be well transmitted to the left axilla, suggest-

mitted out along the pulmonary artery rather than arising from the mitral valve The presence of a thrill is helpful, not only in locating a point of maximal intensity of a murmur, but in evaluating distribution.

DURATION AND QUALITY. In the presence of aortic and pulmonary stenosis, a *long murmur,* which occupies all of systole, suggests that stenosis is severe A *short systolic murmur,* on the other hand, indicates that the ventricle empties relatively rapidly and, therefore, that the stenosis is not severe. A *high-pitched murmur* indicates markedly increased velocity of blood flow through a defect or a point of obstruction. High velocity can occur only if the pressure differential is great. Consequently, a high-pitched systolic murmur would suggest a pulmonary or aortic stenosis with a high ventricular and low distal artery pressure or a small ventricular defect with normal right and left ventricular pressures.

If a *diastolic murmur* is present, it first must be determined if this murmur is a continuation into diastole of a murmur heard in systole or whether it is separate and distinct The *murmur of a patent ductus arteriosus is continuous.* If the murmur fades out and then starts again with increased intensity in the early part of diastole, it is *to and fro* and not continuous. A *decrescendo diastolic murmur,* either short or long, usually soft and blowing in quality, indicates pulmonary or aortic insufficiency. If arising *from the aortic valve,* the murmur can be heard along both sides of the sternum over the base of the heart and down toward the xiphoid process If it arises *from the pulmonary valve,* it is usually not heard to the right of the sternum near the xiphoid process A common diastolic murmur is an *early, low-pitched diastolic sound located along the left sternal border.* The etiology of this murmur is obscure, but it is associated with a large and greatly overworked heart A *mid-diastolic rumble* out toward the apex or between the apex and the sternum suggests a relative mitral or tricuspid stenosis It is common in lesions causing a high return of blood to the left atrium, such as a patent ductus arteriosus or ventricular septal defect and also in patients with an atrial septal defect who have a large volume of blood passing from a large right atrium into a large right ventricle

EXTRACARDIAC MURMURS In patients with severe pulmonary stenosis, *collateral vessels to the lungs* may cause a *blowing continuous murmur,* heard over both chests anteriorly and posteriorly but not maximally over the 2d left interspace A *low-pitched continuous bruit* may also be heard in coarctation of the aorta because of collateral *circulation in the chest* wall A *midsystolic murmur,* not particularly loud and poorly localized, heard well over the back and over the base of the heart, is the usual murmur associated with coarctation of the aorta. A *continuous murmur* or *pure sys-*

terior oblique, and if the interventricular groove can be seen in the left anterior oblique position, the groove will lie abnormally far posteriorly. *Enlargement of the left ventricle* tends to make the heart assume a more vertical position, with the long axis of the heart lying at a 45° angle rather than horizontally. The apex of the heart does not clear the diaphragm on deep inspiration, and in the LAO view there is posterior rounding of the ventricle and a reduction of the retrocardiac space. However, if there is marked enlargement of either the right or left ventricle, the opposite ventricle may be displaced in such a way that it appears enlarged. *Right atrial enlargement* is best determined in the LAO and PA views. In the LAO view, a shelf may be seen extending from the pulmonary artery anteriorly toward the chest wall, representing an enlarged right auricular appendage. In the PA projection, cardiac rounding to the right of the spine suggests *enlargement of the right atrium*. *Enlargement of the left atrium* is determined by a study of the barium-filled esophagus and the position of the left main stem bronchus. Elevation of the left main stem bronchus when seen in the LAO view indicates left atrial enlargement. The barium-filled esophagus over a short distance will be displaced to the right in the PA projection when the left atrium is enlarged.

What is the origin, position, course, and size of the two great vessels arising from the heart? The answer to this question is frequently difficult since vessel origin may appear displaced because of rotation of the entire heart. Right ventricular enlargement tends to rotate the heart in a clockwise manner when looked on from below. In so doing, the main pulmonary artery segment is accentuated and the ascending aorta becomes less apparent. When the left ventricle is enlarged, rotation in a counterclockwise fashion occurs. This tends to bring the origin of the pulmonary artery anteriorly and thus make the main pulmonary artery shadow as seen in the PA view concave. In a similar manner, the ascending aorta becomes more prominent. Rotation of the heart can be compensated for by careful rotation of the patient under the fluoroscopic screen. Thus, a full main pulmonary artery segment lying anteriorly because of clockwise rotation of the heart will appear convex and large by rotation into the RAO view. If heavy pulmonary vascular markings are present in the peripheral lung fields, if a large right and left pulmonary artery are visualized, and if in the PA projection the pulmonary artery is concave and does not become concave on rotation into the RAO view, it is probable that the *origin of the pulmonary artery is anatomically displaced.*

A word of caution should be given against excessive reliance on *evaluation of pulmonary vascular markings*. The increased collateral circulation to the lungs in the presence of severe pulmonary stenosis can be mistaken for increased vascularity. Pulsations in the pulmonary vessels do not of necessity indicate increased pulmonary blood flow. Pulsations are dependent upon the thickness of the vessel wall and the amplitude of pulse pressure, as well as the volume of blood flow. The apparent size of the pulmonary vessels and the number of vessels seen on x-ray theoretically should indicate whether flow or pressure to the lung is increased or decreased. However, technical differences in obtaining and developing the x-ray may emphasize or deemphasize the vascular markings, leading to a wrong interpretation. Except when the changes are marked, evaluation of the pulmonary vascular markings is frequently in error.

The course and size of the *aorta* are best determined by a study of the barium-filled esophagus. The presence of a *right aortic arch* is suggested if the aorta is seen pushing the esophagus to the left in the PA projection and posteriorly in the LAO view. The normally positioned aorta deflects the esophagus to the right in the PA projection and posteriorly in the LAO view. In the presence of a *coarctation of the aorta*, careful examination of the patient in the LAO view may reveal the presence of a dilated segment of aorta immediately distal to the coarctation. Dilatation of the ascending aorta suggests *aortic stenosis*. A dilated ascending aorta with a definite incisura at the point where the right atrium overlaps the aorta in the PA projection is good evidence of *valvular aortic stenosis*, whereas a dilated aorta with complete blending of right atrial and aortic shadows without incisura suggests *subaortic stenosis*.

What is the activity of the heart and great vessels? In the presence of a large left-to-right ventricular shunt, the activity of both right and

tolic murmur may be heard over one or both lung fields, arising from single or multiple coarctations of the pulmonary artery branches.

SECOND HEART SOUND. A *split 2d sound* suggests that both aortic and pulmonary valves are functioning, and hence a severe valvular pulmonic or aortic stenosis is not present. A *quiet 2d sound* to the left of the sternum suggests a decreased pulmonary blood flow. However, it must be remembered that, in the presence of a tetralogy of Fallot, the position and size of the aorta accentuate the aortic 2d sound in the 2d *left* interspace In this condition, a loud pure 2d sound in the 2d left interspace does not rule out decreased pulmonary blood flow An *accentuated* and *split 2d sound* suggests increased pulmonary blood flow probably associated with increased pulmonary pressure

Examination of Lungs. Rales, inspiratory and expiratory wheezes, may be present in patients with congestive heart failure as well as with pulmonary infections In infants, however, rales may not be present even when failure is severe Decreased breath sounds over the left base posteriorly suggest marked enlargement of the left side of the heart with *compression atelectasis* of the left lower lobe This is an infrequent finding when cardiac enlargement is of the right side alone In evaluating the chest, it is well to listen twice, once for murmurs and secondly for abnormal pulmonary sounds

Abdomen. The size and character of the liver are of primary importance in the examination of the abdomen In infancy, the liver characteristically can be felt 1 to 3 cm below the right costal margin Under such circumstances, evaluation of the liver rests upon the consistency of the edge that is palpable rather than size. A sharp firm edge indicates hepatic congestion An enlarged spleen may be palpated in patients with cyanotic congenital heart disease As a general rule, the greater the degree of polycythemia, the more likely one is to feel an enlarged spleen

X-RAY AND FLUOROSCOPY

To obtain the maximum amount of information, the fluoroscopic examination should be carried out by the examiner who has taken the history and done the physical examination, as well as by the radiologist. It is only in this way that sufficient attention can be given to differential points. *In infancy, the fluoroscopic examination is vastly more informative than the x-ray examination*

An infant's rapid respirations make it difficult to obtain a roentgenogram at the peak of inspiration when the diaphragm is lowest and the mediastinal shadow the narrowest. More important, some degree of rotation of the chest is almost always present. Rotation accentuates the wide mediastinal shadow normally present and obscures the contour of the heart. It should be the policy to obtain x-rays on the small infant in order to have a permanent record for comparison with films taken at an older age, but the findings by x-ray are not accepted as accurate unless they have been confirmed by a fluoroscopic examination.

In general, the fluoroscopic and x-ray examination of the heart should be aimed at answering the following questions·

Is the heart normal in size or enlarged? Evaluation of the heart size in the small infant is difficult because the heart lies transversely because of a high diaphragm, and thus, in the posteroanterior view, its width is increased As a child grows and the chest lengthens, the diaphragm assumes a lower position. The heart tends to be in a more vertical plane, and the ratio of width of heart to width of chest is more significant. Despite the difficulty of absolute measurement of heart size in a small child, an impression of size can be gained which may be helpful in establishing a diagnosis. The heart of a child with pulmonary stenosis and a ventricular septal defect tends to be *small*, whereas that of a child with a transposition of the great vessels tends to be *increased in size* Thus, when cyanosis is present, an impression of the heart size is helpful in differentiating the malformations. In noncyanotic patients with defects between the two sides of the heart, the heart size gives some indication of volume of flow through the defect. When pulmonary resistance is high and pulmonary blood flow low, heart size tends to be within normal limits, but when the pulmonary resistance is low and the volume of shunt from left to right through the defect is large, the *heart size is increased.*

What specific cardiac chambers have been altered in size and contour? The *enlarged right ventricle* tends to enlarge the heart transversely in the PA projection, anteriorly in the right an-

The "systolic" and "diastolic overload" patterns have been of definite help in differential diagnosis.

The degree of *right ventricular hypertrophy*, as determined by the ECG, is of value in differential diagnosis, as well as in determining the magnitude of stress placed on the heart. In the presence of pulmonary stenosis with a large ventricular septal defect (*tetralogy of Fallot*), the right ventricle must develop sufficient contractile strength to force blood out through the stenotic pulmonary orifice or through the ventricular defect into the aorta. Because of the ventricular defect, the maximum required work of the right ventricle is merely enough work to overcome systemic resistance As a consequence, the degree of hypertrophy is not great. On the other hand, when there is *pulmonic stenosis with an intact ventricular septum*, the right ventricle has no escape valve and must overcome the resistance offered by the stenotic pulmonary valve When stenosis is severe, marked right ventricular hypertrophy of the systolic overload form is present in the ECG. A right ventricular strain pattern is common in this malformation but extremely rare in patients with the typical tetralogy of Fallot.

Systolic overload of the left ventricle is characterized by an S in V_1 plus an R in V_5 and V_6 of more than 35 mm The interval from Q to the peak of the intrinsicoid deflection in the left precordial leads is greater than 0 05 sec The *left ventricular diastolic overload* pattern is characterized by elevation of the S-T segment in leads facing the left ventricle and an upright, peaked T wave. These patterns are less clear-cut than similar patterns for the right ventricle, and hence, their value in differential diagnosis is less reliable.

Some evidence concerning stress placed on the atria can be obtained from the ECG A tall, peaked P wave in leads II, III, aVF, and over the right chest leads suggests *right atrial enlargement and hypertrophy*. A notched P wave in leads I, II, aVL, a diphasic P wave in V_1, and a large P wave with a short P-R interval over the chest leads is evidence of *left atrial enlargement and hypertrophy*.

There are serious pitfalls in the interpretation of the ECG. An abnormal position or unusual rotation of the heart alters the electrocardiographic pattern and may suggest an incorrect diagnosis. Unusual conduction disturbances may be mistaken for hypertrophy patterns. *Failure of one ventricle* may be associated with a decrease in electrical activity and relative preponderance of the other ventricle in the ECG. Such a pattern has been described in patients with extreme valvular pulmonary stenosis where there is a greatly dilated and thin-walled right ventricle associated with electrocardiographic evidence of left ventricular preponderance.

One point of diagnosis should be strongly emphasized: the clinical findings and laboratory results must all fit together and direct attention toward the correct diagnosis. If there are discrepancies, an explanation for the discrepancies must be given, or the diagnosis may well prove wrong.

CLASSIFICATION OF CONGENITAL HEART DISEASE

The classification of congenital heart disease presented here is divided into two parts In part one (outline at beginning of chapter), the *classification is based upon the type of defect* without reference to whether pulmonary stenosis or pulmonary vascular disease complicates the defect and without reference to the direction of the shunt In part two (Table 6-1), the *factors which control the clinical picture presented by specific malformations are correlated and analyzed*. Each group of defects will be discussed first as a unit, with emphasis placed on the alterations in hemodynamics produced by the size of the defect and by varying degrees of pulmonary stenosis or pulmonary vascular disease (right ventricular outflow obstruction). The purpose of doing this is not only to save repetition, but to emphasize that, from the physiologic standpoint, a large patent ductus arteriosus is essentially the same as a large ventricular defect, and a ventricular septal defect associated with severe pulmonary stenosis (tetralogy of Fallot) is similar to a large ventricular defect with advanced pulmonary vascular disease (Eisenmenger's syndrome). Once having established the similarities within each group, the differential diagnostic points can be brought out in a discussion of each specific malformation

The estimated frequency of clinical syndromes for each defect is presented in Table 6-2.

left ventricle and pulmonary arteries is increased. *If the shunt is at the atrial level*, the activity of the heart (in the left oblique) is increased anteriorly, but not posteriorly, suggesting that the right ventricle is handling a greater volume of blood than normal. When a *patent ductus* is present, both the ascending aorta and pulmonary artery may be quite active. If, however, the defect is intracardiac and the shunt from left to right, the aorta appears quiet and smaller than normal. *Tricuspid insufficiency* is suggested by increased activity [illegible]

[illegible] the RAO view.

In contrast to the actively pulsatile pulmonary vessels and heart of a patient with a large left-to-right shunt, *pulmonary stenosis, aortic stenosis*, and marked *pulmonary vascular disease* are characterized by a decreased cardiac activity. In patients with an *anomalous left coronary artery* arising from the pulmonary artery or with *endocardial fibroelastosis*, the left ventricle, although large, is strikingly quiet. *Aortic stenosis* is suggested by a delayed and slow pulse wave of the ascending aorta. *Aortic insufficiency* or a left-to-right shunt between the aorta and pulmonary artery is suggested by rapid filling and emptying of the aorta, with an accentuation of the aortic pulsations.

ELECTROCARDIOGRAM

A few general principles of electrocardiography will be discussed in this chapter; a more detailed analysis may be found in Chap. 5.

In the newborn baby, the right and left ventricles are of equal thickness and equal size, a fact which is in keeping with the equality of the load that each ventricle must bear during fetal life. The ECG of the *newborn* is characterized by the patterns called *right axis deviation* or *right ventricular preponderance*. In actuality such a pattern, seen when both ventricles are anatomically equal, must represent a true balance, or electrical equality of [illegible]

[illegible] in V_5 as indicative of a balance between the two ventricles. The *normal adult pattern indicates not a true balance, but left ventricular preponderance*. With this in mind, the electrocardiographic pattern in childhood becomes of diagnostic aid. A continuation of the normal newborn pattern into childhood suggests that the work load of each ventricle, equal in fetal life, has continued unchanged after birth. A shift toward the normal adult "balanced" state in early childhood suggests that the *left ventricle has hypertrophied at an accelerated rate* as a result of an increased left ventricular work load. Conversely, an increased right ventricular pattern suggests that *only the right ventricle has an abnormally increased work load*.

Serial ECGs are of great importance not only in diagnosis but in the evaluation of the severity of the condition. Most forms of congenital heart disease do not cause stress during intrauterine life. *Only when the fetal circulation* is altered by the shift in dependence for gaseous exchange from the placenta to the lungs does stress become *manifest*. With the passage of *time*, evidence of hypertrophy of one or both ventricles *appears*, indicating the *presence of increased demand*. The rapidity of the *electrocardiographic change*, furthermore, may serve as an index to the severity of the *condition*.

It is possible to differentiate the type of stress placed on a ventricle. For example, in the presence of a simple *atrial septal defect*, the right ventricle has a markedly *increased* volume of blood flow to accommodate, but *resistance to flow* from the right ventricle is not usually increased. The typical pattern of the ECG (*diastolic overload of the right ventricle*) is one in which there is a wide QRS complex over the right chest leads associated with a notched R or an RSR' pattern, and usually not associated with a marked increase in height of the R wave or an inversion of the T wave. In contrast to this pattern, that of *isolated valvular pulmonic stenosis*, in which the stress placed on the right ventricle *is not* an increased volume of blood flow, but rather an increased resistance to outflow (*systolic overload*), is characterized by *excessively* tall R waves over the right chest leads and deep S waves over the left chest leads. When the systolic overload is more severe, inversion of the T wave and depression of the S-T segment are added to the pattern and indicate *right ventricular strain*.

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[illegible] when the systolic overload is more severe, inversion of the T wave and depression of the S-T segment are added to the pattern and indicate *right ventricular strain*

GROUP I: LARGE DEFECTS BETWEEN THE VENTRICLES OR GREAT VESSELS

The left and right ventricle function as a *single pump* with a common ejectile force, if the defect is functionally large. The volume of blood flow to the systemic and pulmonary circulation, therefore, is totally dependent upon the peripheral resistance in each. The replacement of fluid by air in the alveoli after birth reduces pulmonary resistance. In contrast to the normal circulation of the newborn, the fetal ratio of pulmonary blood flow to the vascular bed is maintained, for every additional patent pulmonary capillary increases the blood flow tapped from the systemic circulation, and pulmonary hypertension persists. The lungs remain as an integral part of the systemic circulation just as in the fetus, alterations in the vascular resistance affect the entire circulation exactly in the same manner as alterations in the kidney, brain, or mesenteric vessels, and yet the lungs, after birth, contain a vascular bed not well supported by surrounding tissue but literally suspended in air. It is small wonder that the pulmonary vascular bed cannot compete with other parts of the circulation without progressive alterations.

There are three lines along which the pulmonary circulation may develop: (1) The reduction of pulmonary resistance following birth leads to a *progressive increase in pulmonary blood flow.* (2) A *balance is maintained* between the two circulations by injury and the retention of an efficient vascular tone, sufficient to keep pulmonary vascular resistance on a par with systemic vascular resistance. (3) The sudden decrease in extravascular pressure, combined with the persistence of a high intravascular pressure, produces *severe vascular injury,* a pulmonary arteritis, and a progressively increasing pulmonary resistance. Thus, in the presence of a large defect, although pulmonary hypertension is retained following birth, the clinical course can be one of (1) low pulmonary resistance, high pulmonary blood flow, and progressive decompensation; (2) balanced flow and relative lack of symptoms until sufficient injury occurs to the pulmonary vessels to elevate pulmonary resistance; or (3) markedly elevated pulmonary resistance, low pulmonary blood flow, right-to-left shunt, and cyanosis.

Large Defect between the Ventricles or Great Vessels with Minimal Right Ventricular Outflow Obstruction. With this combination, there is a large left-to-right shunt, a high pulmonary blood flow, and an increased volume of blood returning to the left atrium, causing *enlargement of the left side of the heart.* The *right ventricle is also enlarged* since it is forced to generate a pressure equivalent to the systemic.

The signs and symptoms result from left and right heart strain. Dyspnea, fatigability, orthopnea, increased susceptibility to pulmonary infections, and impaired growth and development are common. If heart failure ensues, the most common presenting sign is pulmonary congestion. The peripheral pulses are usually weak. There is a bulge of the left anterior chest and an increased precordial activity. The heart is grossly enlarged, with an active apical impulse located lateral to the midclavicular line in the 5th and 6th left interspace. Murmurs are variable. A *systolic murmur,* if present, is usually *short, early, low pitched,* and *coarse.* A *mid-diastolic rumble,* heard at the apex, is a common finding The 2d heart sound at the base is *increased* in intensity. Rales may be heard over the chest. The liver is enlarged, and there may be peripheral edema.

By fluoroscopic examination, the *pulmonary vascular markings appear increased and actively pulsatile.* The heart is enlarged, the apex is anteriorly rotated, and the main pulmonary artery segment is less convex than might be expected by the size of the peripheral pulmonary arteries. The apex extends inferiorly and to the left and fails to clear the diaphragm on deep inspiration In the LAO view, there is posterior rounding, suggesting enlargement of the left ventricle, in the RAO view, the heart impinges on the anterior chest wall, suggesting enlargement of the right side of the heart. The barium-filled esophagus deviates posteriorly in the RAO view, indicating enlargement of the left atrium

In the ECG, there are wide swinging QRS complexes with a pattern that is neither purely right nor purely left, thereby suggesting *biventricular enlargement* A notched P wave may be present in leads II, III, and aVF. In the angiocardiogram, there is *reopacification of the pulmonary artery* and minimal opacification of

TABLE 6-2 ESTIMATED FREQUENCY OF CLINICAL SYNDROMES FOR EACH DEFECT: GROUP I

Size of defect	*Degree of pulm stenosis or pulm vascular disease*	*Patent ductus*	*Aortic septal defect*	*Single ventricle*	*Ventricular defect*	*Tetralogy of Fallot*	*Truncus*	*Pseudotruncus*	*Coarctation with proximal PDA*
Large	Mild or absent	2	2	3	3	1	1	0	3
	Moderate	2	3	4	3	4	4	2	3
	Severe	1	3	3	3	3	3	4	3
Medium	Mild or absent	3	3		3	1	1	0	2
	Moderate	1	4		4	3	1	2	4
	Severe	0	3		3	1	1	3	4
Small	Mild or absent	4	3		3	4	0	0	2
	Moderate	1	0		1	1	0	2	3
	Severe	0	0		0	1	0	1	1

Size of defect	*Degree of pulm stenosis or pulm vascular disease*	*Coarctation with distal PDA*	*Single ventricle with transposition*	*Single ventricle with pulmonic stenosis*	*AV communis*	*AV communis with pulmonic stenosis*	*Biloculate heart*	*Biloculate heart with pulmonic stenosis*	*Tricuspid atresia* *
Large	Mild or absent	1	3	1	3	1	3	3	2
	Moderate	3	4	3	3	4	3	4	.
	Severe	4	3	4	3	3	4	3	
Medium	Mild or absent	1			3	1			
	Moderate	4			4	4			4
	Severe	4			3	3			
Small	Mild or absent	2			2	1			
	Moderate	1			2	1			
	Severe	0			1	1			3

Size of defect	*Degree of pulm stenosis or pulm vascular disease*	*Tricuspid atresia with transposition*	*Transposition with PDA*	*Transposition with ventricular septal defect*	*Taussig-Bing*	*Aortic atresia with PDA*	*Aortic and mitral atresia with PDA*	*Mitral atresia and ventricular septal defect*	*Mitral stenosis with PDA*	*Mitral stenosis with VSD*
Large	Mild or absent	3	1	3	0	0	0	0	0	0
	Moderate	4	2	4	4	3	3	3	3	3
	Severe	3	2	3	3	4	4	4	4	4
Medium	Mild or absent	1	1	2	0	0	0	0	0	0
	Moderate	.	4	4	3	3	3	3	3	3
	Severe		3	3	2	3	3	3	3	3
Small	Mild or absent		1	1	1	0	0	0	0	0
	Moderate	.	3	2	1	3	3	3	3	3
	Severe	3	2	1	3	3	3	3	3	3

* Pulmonary stenosis caused by size of ventricular defect or patent ductus arteriosus.
Key: 4, most common, 3, common; 2, less common; 1, rare; 0, not seen

the degree of pressure drop. A low-pitched, coarse, and short systolic murmur suggests a minimal pressure differential. A high-pitched jetlike systolic murmur suggests a high pressure differential.

Fluoroscopic evidence of left ventricular and left atrial enlargement is present. Right ventricular enlargement is variable. The ECG suggests more left ventricular enlargement than right. Angiocardiography indicates reopacification of the pulmonary arteries. Cardiac catheterization demonstrates the difference in pressure between the systemic and pulmonary circulations. Otherwise the findings are similar to those of a large defect

Medium-sized Defect with Moderate Right Ventricular Outflow Obstruction. This combination undoubtedly exists but cannot be differentiated from a large defect with moderate outflow tract obstruction The resistance offered by the pulmonary valve or the small pulmonary vessels is of sufficient magnitude to reduce the volume of pulmonary blood flow to the point where the resistance offered by the defect is no longer manifest and ventricular pressures are equal The pressure drop occurs across the pulmonary valve or the pulmonary vascular bed and not across the defect. The clinical picture is that of a large defect associated with moderate right ventricular outflow obstruction.

Moderate-sized Defect with Marked Right Ventricular Outflow Obstruction. This combination cannot be differentiated from a large defect associated with severe right ventricular outflow obstruction The resistance offered by the pulmonary arterial bed or pulmonary valve area limits the shunt to a much greater degree than the defect itself. Consequently, the pressures within the right and left side are equal

Small Defect with Minimal Right Ventricular Outflow Obstruction. In this combination, the principal resistance to a left-to-right shunt is the size of the defect *Pressures approach normal in the right side of the heart* since the defect offers the chief barrier. The left side of the heart has an increased work load because of the left-to-right shunt, and some left ventricular enlargement may be present. Symptoms are lacking since the volume of shunt is so small that the heart and lungs are not sufficiently embarrassed. Physical examination reveals a well-developed and well-nourished individual with normal peripheral pulses, no bulge to the left chest, minimal or absent cardiac enlargement, and normal precordial activity. The outstanding findings are auscultatory. Since pressures in both circulations are normal, the flow of blood across the defect is at high velocity, causing a *loud, long, high-pitched systolic murmur* heard best along the left sternal border in the 4th and 5th left interspace. Evidence of failure is not present. Fluoroscopic examination reveals a normal heart or one with minimal left-sided enlargement The pulmonary vascular markings are slightly increased and overly pulsatile. The ECG usually is normal. Some evidence of reopacification of the pulmonary circulation may be present in the angiocardiogram Cardiac catheterization establishes the presence of *normal pressures in the two sides of the heart,* and *a rise in oxygen content is found at the level of the defect.*

Small Defect with Moderate Right Ventricular Outflow Obstruction. A small defect associated with moderate pulmonary stenosis is an unusual combination. A small defect associated with moderate pulmonary vascular disease is seen occasionally in older patients in whom the available pulmonary vascular bed has been reduced by pulmonary parenchymal disease The increased work load is primarily on the right ventricle Exertional dyspnea is common *Cyanosis may appear with exercise.* Physical findings are dependent upon the degree of pulmonary stenosis or pulmonary vascular disease Since the shunt is reduced by the pulmonary resistance and not by the defect, the murmur arising from the defect is not present A loud, long, high-pitched systolic murmur is present if the increased pulmonary resistance is at the valve.

Small Defect with Marked Right Ventricular Outflow Obstruction. This combination is very rare The degree of resistance in the pulmonary vascular bed or at the pulmonary valve places a heavy load on the right side of the heart which, in this instance, cannot be reduced sufficiently by the right-to-left shunt through the excessively small defect The right side of the heart is enlarged, perhaps markedly so. Signs and symptoms are dyspnea, marked fatigability, occasional spells of paroxysmal dyspnea, cyanosis that may be marked, and evidence of right heart failure On physical examination, the findings are those of isolated pulmonary obstruction with intact ventricular sep-

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Size of defect	*Degree of pulm. stenosis or pulm vascular disease*	*Patent ductus*	*Aortic septal defect*	*Single ventricle*	*Ventricular defect*	*Tetralogy of Fallot*	*Truncus*	*Pseudotruncus*	*Coarctation with proximal PDA*	*Coarctation with distal PDA*	*Single ventricle with transposition*	*Single ventricle with pulmonic stenosis*	*AV communis*	*AV communis with pulmonic stenosis*
Large	Mild or absent	2	2	3	3	1	1	0	3	1	3	1	3	1
	Moderate	2	3	4	3	4	4	2	3	3	4	3	3	4
	Severe	1	3	3	3	3	3	4	3	4	3	4	3	3
Medium	Mild or absent	3	3		3	1	1	0	2	1			3	1
	Moderate	1	4		4	3	1	2	4	4			4	4
	Severe	0	3		3	1	1	3	4	4			3	3
Small	Mild or absent	4	3		3	4	0	0	2	2			2	1
	Moderate	1	0		1	1	0	2	3	1			2	1
	Severe	0	0		0	1	0	1	1	0			1	1

Size of defect	*Degree of pulm. stenosis or pulm vascular disease*	*Bilocular heart*	*Bilocular heart with pulmonic stenosis*	*Tricuspid atresia* *	*Tricuspid atresia with transposition*	*Transposition with PDA*	*Transposition with ventricular septal defect*	*Taussig-Bing*	*Aortic atresia with PDA*	*Aortic and mitral atresia with PDA*	*Mitral atresia and ventricular septal defect*	*Mitral stenosis with PDA*	*Mitral stenosis with VSD*
Large	Mild or absent	3	3	2	3	1	3	0	0	0	0	0	0
	Moderate	3	4		4	2	4	4	3	3	3	3	3
	Severe	4	3		3	2	3	3	4	4	4	4	4
Medium	Mild or absent				1	1	2	0	0	0	0	0	0
	Moderate			4		4	4	3	3	3	3	3	3
	Severe					3	3	2	3	3	3	3	3
Small	Mild or absent					1	1	1	0	0	0	0	0
	Moderate					3	2	1	3	3	3	3	3
	Severe			3	3	2	1	3	3	3	3	3	3

* Pulmonary stenosis caused by size of ventricular defect or patent ductus arteriosus.
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the aorta Catheterization findings are those of a large left-to-right shunt at or distal to the ventricles, minimal or absent right-to-left shunt, equal systolic pressures in the right ventricle and brachial artery, and elevated pulmonary wedge pressures.

Large Defect with Moderate Right Ventricular Outflow Obstruction. When there is a moderate obstruction to right ventricular outflow, the resistance to blood flow through the lungs approximates the resistance to blood flow through the systemic circulation, and *flows are essentially equal* The left side of the heart is normal The right ventricle is increased in size because it must generate a pressure equal to that of the left ventricle. Signs and symptoms are mild or absent There may be mild exertional dyspnea and, with severe exercise, some degree of cyanosis. Growth and development are within normal limits. On physical examination, the peripheral pulses are normal There is no bulge of the precordium, and the heart is approximately normal in size Precordial activity may be increased. There may be a short early-systolic murmur. There is no evidence of cardiac failure.

On fluoroscopy, the left atrium and the left ventricle are normal In the oblique views, there is a suggestion of right ventricular enlargement. In the ECG, there is *right axis deviation* and evidence of moderate right ventricular hypertrophy An angiocardiogram may fail to demonstrate any shunt, or there may be reopacification of the pulmonary artery and early visualization of the aorta, indicating both a left-to-right and right-to-left shunt. An equal right ventricular and brachial artery systolic pressure is demonstrated by catheterization. There is usually *some degree of arterial unsaturation* and a slight increase of right ventricular blood oxygen content Pulmonary wedge pressures are normal

Large Defect with Severe Right Ventricular Outflow Obstruction. When this combination is present, the findings are due to a *markedly reduced pulmonary blood flow.* The left ventricle is normal in size The right ventricle is increased in size because of the increase in resistance to ventricular outflow Symptoms include cyanosis, exertional dyspnea, and marked fatigability Growth and development are retarded. *Cyanosis and clubbing are present* Peripheral pulses are normal The right ventricle may appear slightly enlarged. *Murmurs are variable,* depending upon the exact nature of the defect. The chest is clear. Evidence of cardiac failure is absent. On fluoroscopy, there is evidence of right ventricular enlargement. In the ECG, there is *right axis deviation* and *right ventricular hypertrophy,* without evidence of left ventricular hypertrophy. An angiocardiogram reveals *early opacification of the aorta* and *delayed filling of the pulmonary arterial tree.* Catheterization findings are those of a *common systolic pressure in the right ventricle and brachial artery* and *marked arterial unsaturation.*

Moderate-sized Defect with Minimal Right Ventricular Outflow Obstruction. A moderate-sized defect is defined as one large enough to permit a sufficient volume of blood flow to utilize most of the available pulmonary vascular bed, yet small enough to limit blood flow by its size. Thus, the volume of pulmonary blood flow is controlled by both the resistance offered by the pulmonary circulation and the resistance offered by the defect. The medium-sized defect associated with minimal pulmonary stenosis or pulmonary vascular disease causes a left-to-right shunt since the resistance of the lungs and of the defect is significantly less than the resistance of the systemic circulation

The signs and symptoms differ only in degree from those of a large defect associated with minimal outflow obstruction The left side of the heart is enlarged because of increased return of blood to the left atrium and left ventricle The degree of right-sided enlargement varies directly with right ventricular pressure. Symptoms are fatigability, exertional dyspnea, and susceptibility to pulmonary infections

The difference in cardiac findings between this group and the group with a large defect depends upon the pressure drop across the defect Examination of the precordium may suggest that the left ventricle is performing more work than the right. There is a forceful and diffuse apical impulse which is more active than the right ventricular impulse close to the sternum The apex is lower and more to the left, indicating *left ventricular enlargement.* There is a *systolic murmur,* which is caused by rapid blood flow through the defect. The quality and duration of the murmur depend upon

tricular defect (maximal in early systole). The *pulmonary 2d sound is split and loud. A diastolic murmur, faint and blowing and decrescendo in type,* may be present along the left sternal border. A mid-diastolic rumble resulting from a large return of blood to the left ventricle may be present at the apex. On fluoroscopy, the presence of both an enlarged hyperactive ascending aorta and pulmonary artery suggests that the shunt occurs distal to the ventricles. Angiocardiogram in the left oblique view may suggest the presence of an intermittent right-to-left shunt by opacification of the descending aorta as well as reopacification of the pulmonary artery. Cardiac catheterization reveals a *high pulmonary artery pressure* and a *rise in the oxygen content distal to the pulmonary valve* The diagnostic value of the oxygen content rise may be obscured by the presence of pulmonary insufficiency, leading to a rise in oxygen content in the outflow tract of the right ventricle. The most efficient differential diagnostic test for this syndrome is a *retrograde aortogram* Contrast medium injected under pressure into the left brachial artery in a retrograde manner will opacify the pulmonary arteries immediately

Large Patent Ductus Arteriosus with Marked Pulmonary Vascular Disease. This, the *reverse ductus,* is usually not seen until late in life. The *flow is from right to left because of the high pulmonary resistance.* Differential diagnostic findings are related to the position of the shunt since the ductus communicates with the aorta at, or just distal to, the origin of the left subclavian artery. *Cyanosis of the lower extremities and left hand is pathognomonic* If the shunt is small in magnitude, no cyanosis is present, but simultaneous oxygen determinations from the right brachial and femoral arteries reveal a *lower saturation in the femoral artery than in the brachial* Angiocardiogram in the left oblique position may suggest early opacification of the descending aorta

THERAPY. Therapy for the typical variety of patent ductus arteriosus is, with few exceptions, surgical closure When the ductus is large and pulmonary vascular disease moderate or mild, early closure is mandatory, for only in this way can a progressive increase in pulmonary resistance be prevented. Furthermore, when left heart failure is present, closure can be lifesaving. The question of closure of a reverse ductus is difficult. Closure is indicated if it can be established that the right-to-left shunt through the defect can be eliminated or greatly reduced by breathing 100 per cent oxygen or if the shunt, though bidirectional, is predominantly left to right.

Moderate Aortic Septal Defect with Moderate Pulmonary Vascular Disease. In this malformation, there is a communication between the aorta and pulmonary artery just distal to the aortic and pulmonary valve. The distinguishing diagnostic features of a moderate-sized septal defect are few. A *systolic murmur, maximal in the 3d left interspace* and extending slightly into diastole, is suggestive. The first portion of the ascending aorta and main pulmonary artery is usually markedly dilated. Cardiac catheterization is of little help unless the catheter can be passed through the defect into the aorta and innominate artery, thus distinguishing the defect from a patent ductus arteriosus. However, one must be sure that the catheter did not pass through a ventricular defect to the aorta rather than through an aortic septal defect. Angiocardiography will reveal opacification of the ascending aorta as well as the descending aorta, which serves to distinguish this defect from a reverse ductus. To differentiate this defect from a ventricular defect, a retrograde aortogram, done through the right brachial artery with the right carotid momentarily occluded, will result in a heavy flow of contrast medium into the pulmonary circulation without opacification of the ventricles.

Small Aortic Septal Defect with Minimal Pulmonary Vascular Disease. The findings are those of a patent ductus except that the continuous murmur is audible *lower and more to the right* than is usual with a patent ductus The murmur transmits widely. The differential diagnosis is best made with retrograde aortography, for with an aortic septal defect, when the contrast medium is introduced into the left brachial artery, the lungs will not be opacified. Contrast medium injected into the right brachial artery may opacify the pulmonary vessels but not the ventricles.

THERAPY Correction of an aortic septal defect, if it is to be successful, must be performed during childhood, for pulmonary vascular disease tends to develop early. Surgical closure

tum rather than those of an extreme tetralogy of Fallot The right ventricle is greatly enlarged. There is a precordial bulge, but the precordium is quiet. There is a *loud, high-pitched,* and *jetlike systolic murmur* if the pulmonary obstruction is valvular or infundibular. A systolic murmur arising from the right-to-left shunt through the defect may also be present The lungs are clear. There is evidence of right-sided congestive failure, with enlargement of the liver and peripheral edema. The *liver may pulsate* with a strong presystolic pulsation, indicating marked *right atrial hypertrophy*, and occasionally with systolic pulsations, indicating *tricuspid insufficiency* Fluoroscopic examination reveals a markedly enlarged right ventricle and right atrium Peripheral lung fields appear clear The left side of the heart is normal. The ECG *reveals pure right-sided hypertrophy of the systolic overload type, which is frequently extreme and associated* with right heart strain Angiocardiography reveals a *delayed passage of contrast medium through the pulmonary bed* There may be evidence of right-to-left shunt with early opacification of the aorta Cardiac catheterization findings are those of a *markedly increased right ventricular pressure, increased right atrial pressure,* and a *significant degree of arterial oxygen unsaturation* Venous oxygen saturation in the right side of the heart is low, indicating a low systemic blood flow

ANALYSIS OF SPECIFIC MALFORMATIONS

In Table 6-2 are estimated the relative incidence of the size of defect and degree of pulmonic stenosis or pulmonary vascular disease found in each specific malformation. Conditions associated with pulmonary stenosis of varying degrees have been separated from those associated with pulmonary vascular disease according to the difference in frequency Thus, the most common form of patent ductus arteriosus is a small ductus associated with minimal or absent pulmonary vascular disease. In contrast, the most common form of tetralogy of Fallot is a large or medium-sized ventricular defect associated with marked pulmonary stenosis In the discussion of each specific malformation, the most common form will be discussed first, and emphasis will be placed on the distinguishing diagnostic points separating one malformation from another having a comparable defect size and a similar pulmonary resistance.

Small Patent Ductus Arteriosus with Minimal or Absent Pulmonary Vascular Disease. The usual patent ductus arteriosus is small, 4 to 8 mm in internal diameter and 1 to 2 cm long, connecting the left pulmonary artery and the aorta just distal to the origin of the left subclavian. The volume of the shunt is sharply limited by the ductal size *Pulmonary pressure is within normal limits.* Positive physical findings are late in appearing, so that the patient is usually referred during the second year of life or later. The distinctive physical findings relate to the continuous draining of blood from the aorta into the pulmonary circulation There is a *high systemic pressure with an increased systolic and a definitely lowered diastolic pressure.* Peripheral pulses tend to be bounding in nature There is a *continuous murmur*, maximal in the 2d left interspace, well heard in the 1st, with the diastolic component fading in the 3d and disappearing in the 4th interspace This *reaches its greatest intensity in midsystole and extends throughout diastole* The murmur is [illegible]

[illegible] neck, and is faintly heard in the back *A mid-diastolic rumble at the apex* is evidence of increased blood flow through the mitral valve On fluoroscopy, the main pulmonary artery segment tends to be full and *there is increased activity of both the ascending aorta and the pulmonary artery* In the angiocardiogram, an irregularity of the aorta at the level of the ductus is present, a *filling defect of the pulmonary artery* may be noticed, and there may be reopacification of the pulmonary circulation Cardiac catheterization reveals a *rise in the oxygen content of the blood distal to the pulmonary valve*

Large Patent Ductus Arteriosus with Minimal or Moderate Pulmonary Vascular Disease. This entity is not uncommon during early childhood A high pulse pressure with a bounding and collapsing pulse may be present. Instead of the continuous murmur heard with a small ductus, the only murmur present is a *low-pitched, coarse systolic murmur,* located in the 2d left inte[illegible]

years of age. With this syndrome, the important differential diagnostic point is the localization of the pulmonary obstruction. Frequently, no murmur is present, suggesting pulmonary vascular disease rather than valvular pulmonary stenosis When present, the murmur is frequently low-pitched and coarse and does not suggest a high pressure gradient across the defect or valve. The presence of a loud split 2d heart sound and a diastolic decrescendo murmur along the left sternal border suggests pulmonary hypertension and insufficiency, thus placing the obstruction in the distal pulmonary arteries On fluoroscopic examination, the main pulmonary artery and the peripheral pulmonary arteries may be abnormally large Angiocardiographic studies fail to demonstrate an infundibular chamber and infundibular or valvular stenosis A sudden change from a large to a remarkably small lumen may be noted in the peripheral pulmonary vessels Occasionally, the differential diagnosis between this syndrome and one associated with pulmonary valvular stenosis cannot be made unless catheterization of the right ventricle and pulmonary artery demonstrates the presence or absence of a pressure gradient across the valve

Moderate-sized Ventricular Defect with Minimal to Moderate Pulmonary Vascular Disease. The medium-sized defect may be indistinguishable from a large ventricular defect because of the size of the available vascular bed in the small infant. However, with growth of the child and increase in cardiac output without a comparable increase in the size of the defect, the point is reached when the total available vascular bed no longer is being utilized The resistance offered by the defect limits flow, and a pressure differential between the left and right ventricle appears A loud and long systolic murmur along the left sternal border, maximal in the 4th interspace and associated with a thrill, strongly suggests the presence of a pressure differential from left to right ventricle. This finding is born out by direct pressure measurements during cardiac catheterization

Small Ventricular Defect with Minimal Pulmonary Vascular Disease. This condition, the classic *Roger's disease,* is much less frequent than previously thought. The significant diagnostic finding is the presence of a long, loud, high-pitched systolic murmur associated with a strong systolic thrill along the left sternal border, maximal in the 4th and 5th interspace The murmur is jetlike in quality and suggests a marked pressure differential with a high-velocity blood flow across a defect. The catheterization findings are those of an increase in blood oxygen content in the right ventricular outflow tract associated with a normal right ventricular pressure.

A wide range exists between the small defect and the medium-sized defect. The larger the defect, the greater the shunt, until the point is reached where a major portion of the pulmonary vascular bed is utilized and pulmonary artery pressure, even at rest, is elevated The increasing shunt is paralleled by increasing left ventricular work and by the increasing size of both left ventricle and left atrium. When the point is reached where pulmonary artery pressure rises, the work of the right ventricle is increased and evidence of right ventricular hypertrophy appears.

THERAPY As already pointed out, it is common to see patients with large ventricular septal defects who demonstrate successive syndromes The first, appearing within a few weeks after birth, is that of *high-output failure.* The second, which appears in the second and third year of life, is that of *increasing pulmonary resistance,* decreasing pulmonary blood flow, and gradual clinical improvement. The third (*Eisenmenger's syndrome*) is associated with marked pulmonary vascular disease and is the end result unless therapy removes the stimulus toward progressive vascular disease.

During the first phase of high-output cardiac failure, successful closure using an extracorporeal circulation has been done, but this procedure carries a high risk The palliative approach of creating pulmonary stenosis may be the operation of choice in the very small infant Narrowing the pulmonary artery by 75 per cent of its cross-sectional area produces a significant barrier and reduces pulmonary blood flow to between one and two times systemic blood flow Pulmonary artery pressure falls, thus removing the stimulus toward progressive vascular disease By this method, congestive failure can be successfully treated, and growth and development become normal. In time, the risk of corrective surgery becomes less. Such a course also may be indicated in the presence of a medium-sized ventricular defect with min-

tum rather than those of an extreme tetralogy of Fallot. The right ventricle is greatly enlarged There is a precordial bulge, but the precordium is quiet There is a *loud, high-pitched,* and *jetlike systolic murmur* if the pulmonary obstruction is valvular or infundibular. A systolic murmur arising from the right-to-left shunt through the defect may also be present The lungs are clear There is evidence of right-sided congestive failure, with enlargement of the liver and peripheral edema The *liver may pulsate* with a strong presystolic pulsation, indicating marked *right atrial hypertrophy,* and occasionally with systolic pulsations, *indicating tricuspid insufficiency* Fluoroscopic examination reveals a markedly enlarged right ventricle and right atrium Peripheral lung fields appear clear The left side of the heart is normal The ECG reveals pure right-sided hypertrophy of the systolic overload type, which is frequently extreme and associated with right heart strain Angiocardiography reveals a *delayed passage of contrast medium through the pulmonary bed* There may be evidence of right-to-left shunt with early opacification of the aorta. Cardiac catheterization findings are those of a *markedly increased right ventricular pressure, increased right atrial pressure,* and a *significant degree of arterial oxygen unsaturation* Venous oxygen saturation in the right side of the heart is low, indicating a low systemic blood flow

ANALYSIS OF SPECIFIC MALFORMATIONS

In Table 6-2 are estimated the relative incidence of the size of defect and degree of pulmonic stenosis or pulmonary vascular disease found in each specific malformation. Conditions associated with pulmonary stenosis of varying degrees have been separated from those associated with pulmonary vascular disease according to the difference in frequency Thus, the most common form of patent ductus arteriosus is a small ductus associated with minimal or absent pulmonary vascular disease In contrast, the most common form of tetralogy of Fallot is a large or medium-sized ventricular defect associated with marked pulmonary stenosis In the discussion of each specific malformation, the most common form will be discussed first, and emphasis will be placed on the distinguishing diagnostic points separating one malformation from another having a comparable defect size and a similar pulmonary resistance.

Small Patent Ductus Arteriosus with Minimal or Absent Pulmonary Vascular Disease. The usual patent ductus arteriosus is small, 4 to 8 mm in internal diameter and 1 to 2 cm long, connecting the left pulmonary artery and the aorta just distal to the origin of the left subclavian The volume of the shunt is sharply limited by the ductal size. *Pulmonary pressure is within normal limits.* Positive physical findings are late in appearing, so that the patient is usually referred during the second year of life or later. The distinctive physical findings relate to the continuous draining of blood from the aorta into the pulmonary circulation There is a *high systemic pressure with an increased systolic and a definitely lowered diastolic pressure* Peripheral pulses tend to be bounding in nature. There is a *continuous murmur,* maximal in the 2d left interspace, well heard in the 1st, with the diastolic component fading in the 3d and disappearing in the 4th interspace. This *reaches its greatest intensity in midsystole and extends throughout diastole* The murmur is typically *rumbling* and *coarse* It is transmitted laterally toward the left axilla, is not well transmitted into the neck, and is faintly heard in the back. A *mid-diastolic rumble at the apex* is evidence of increased blood flow through the mitral valve On fluoroscopy, the main pulmonary artery segment tends to be full and *there is increased activity of both the ascending aorta and the pulmonary artery* In the angiocardiogram, an irregularity of the aorta at the level of the ductus is present, a *filling defect of the pulmonary artery* may be noticed, and there may be reopacification of the pulmonary circulation Cardiac catheterization reveals a *rise in the oxygen content of the blood distal to the pulmonary valve.*

Large Patent Ductus Arteriosus with Minimal or Moderate Pulmonary Vascular Disease. Th [illegible]

[illegible]

[illegible] pulse may be present Instead of the continuous murmur heard with a small ductus, the only murmur present is *a low-pitched, coarse systolic murmur,* located in the 2d left interspace, which occasionally overlaps into diastole It is maximal in midsystole, which distinguishes it from the murmur of a ven-

midline, and if the pulmonary artery is intubated, the origin of the pulmonary artery may be demonstrated in the midline and posteriorly. Unfortunately, it is frequently impossible to catheterize a great vessel. The remaining laboratory findings suggest the presence of a ventricular defect usually of medium or large size.

THERAPY. The significant lesion to be treated is the ventricular defect, and the same criteria of management apply to this malformation as to the uncomplicated ventricular defect. No special treatment for the transposition is necessary

Tetralogy of Fallot. In this malformation, the ventricular septal defect is associated with infundibular or valvular pulmonary stenosis, an overriding aorta, and right ventricular hypertrophy. The clinical picture is governed by the size of the ventricular defect and the degree of stenosis With rare exceptions, the degree of overriding of the aorta does not affect the patient's symptoms.

Tetralogy of Fallot, Large Defect with Moderate Pulmonary Stenosis. This combination produces dyspnea and cyanosis early in childhood. The diagnostic findings are a *systolic thrill* in the 2d and 3d left interspace associated with a long, high-pitched *systolic murmur,* which is well transmitted over the lung fields. The quality of the murmur suggests a high pressure gradient The *pulmonary 2d sound is usually pure and soft.* However, because of dextroposition of the aorta, the 2d heart sound may be increased at the left of the sternum (the area where the pulmonary 2d sound is usually heard). Diastole is clear Evidence of failure is lacking *Fluoroscopic examination* presents a rather characteristic picture: a small horizontally positioned heart with a blunt, upturned apex which clears the diaphragm is seen in the PA projection The *main pulmonary artery segment is concave* The right and left pulmonary arteries are normal in size. The *peripheral vascular markings are usually decreased.* Minimal pulsations may be seen in the pulmonary vessels. A barium swallow indicates the position of the aortic arch. In about 25 per cent of patients with a tetralogy of Fallot, there is *a right aortic arch,* which deviates the esophagus toward the left in the PA projection and posteriorly in the LAO projection. With a left aortic arch, the esophagus is deviated to the right at the level of the arch and posteriorly in the RAO position. Occasionally, there is a bulge of the left upper cardiac salient or at a little below the level of the main pulmonary artery segment. Pulsations in this area are fairly marked and may appear opposite the ventricular pulsations. This *bulge represents an infundibular chamber* between the area of stenosis and the pulmonary valve.

When the pulmonary artery is catheterized, a drop in pressure (gradient of pressure) is demonstrated from the systemic right ventricle to the infundibular area or pulmonary artery. Pulmonary artery pressure is normal A small left-to-right shunt at the ventricular level may be present, and there is arterial unsaturation It may be possible to distinguish with an angiocardiogram whether stenosis is predominantly infundibular or valvular

Tetralogy of Fallot, Large Defect with Severe Pulmonary Stenosis or Pulmonary Atresia (Pseudotruncus Arteriosus). When this combination is present, the major portion of pulmonary blood flow reaches the lungs through collateral vessels arising from the bronchial vessels, the subclavian arteries, the internal mammaries, and occasionally from below the diaphragm. Symptoms are those of extreme fatigability, dyspnea, and cyanosis. In infancy, many patients are subject to repeated spells of *paroxysmal dyspnea,* characterized by a sudden unexplained increase in cyanosis, gasping irregular respirations, a cry of severe pain, and at times, *loss of consciousness* On physical examination, the cyanosis is marked. A *systolic murmur,* which is high in pitch and moderately long, is heard loudest in the 2d and 3d left interspace Occasionally *no murmur* is present, suggesting either that there is an atresia of the outflow tract of the right ventricle, or that severe polycythemia has increased blood viscosity and decreased the turbulence of blood as it passes through the area of stenosis, therefore making a previously audible murmur inaudible In the severely cyanotic patient, a careful examination for extracardiac murmurs should be made for, not infrequently, a *soft, continuous humming murmur* will be heard over the back, in the axilla, and to the right and left of the sternum anteriorly This murmur arises from large tortuous collateral vessels and not from a patent ductus arteriosus Its presence suggests pulmonary atresia. The 2d heart sound at the base of the heart is pure.

should be performed, using extracorporeal circulation because of the technical difficulty of maintaining coronary circulation and separating the two great vessels by sharp dissection

True Truncus Arteriosus, Large Pulmonary Arteries with Moderate Pulmonary Vascular Disease. This rare malformation is an extension of the aortic septal defect to include a *common aortic and pulmonic valve* and a defect of the ventricular membranous septum Above the common aortic-pulmonic valve arises a *single vessel* which branches rapidly, giving off a right and left pulmonary artery and continues as the aorta Blood flow to the lungs is entirely regulated by the degree of pulmonary vascular disease. In early infancy, pulmonary resistance may be minimal and the occurrence of severe congestive failure is not at all unusual The development of pulmonary vascular disease is rapid, however, and the patient who survives the period of failure passes quickly to the stage of *cyanosis*

The differential diagnosis is obviously difficult. The murmurs are extremely variable The turbulence created by the stream of blood from the right and left ventricles meeting *in a common vessel* causes a *low-pitched, coarse systolic murmur* The common aortic-pulmonic valve is not infrequently *incompetent*, resulting in a decrescendo diastolic murmur heard along both sides of the sternum and a high pulse pressure. These murmurs must be distinguished from the continuous murmur heard in the pseudotruncus arteriosus, where blood flow to the lungs is through collateral vessels arising from the aorta Fluoroscopic examination may reveal an aneurysmal dilatation of the ascending aorta with markedly enlarged right and left pulmonary arteries and a concave main pulmonary segment Cardiac catheterization is of little differential diagnostic value. If the course of the catheter is analyzed carefully, its passage into a pulmonary artery arising from the aorta may be demonstrated Angiocardiography reveals equally rapid opacification of the pulmonary vessels and aorta and an absence of a distinct main pulmonary artery

Correction of this malformation is possible. However, the chances of obtaining a normally functioning aortic and pulmonic valve are poor, and at the present time, our approach is to produce stenosis of the right and left pulmonary arteries to control congestive failure and remove the stimulus to progressive pulmonary vascular disease

Large Ventricular Septal Defect with Minimal or Moderate Pulmonary Vascular Disease. In this malformation, there is a defect between the two ventricles, usually involving the membranous septum and occasionally the muscular septum The defect lies close to the origin of the aorta and may involve the septal leaflet of the aortic valve, thus complicating the hemodynamic changes by the addition of aortic insufficiency. Under the age of 2 years, the most common syndrome is a large ventricular defect associated with mild to moderate pulmonary vascular disease. *Death from high-output cardiac failure is frequent.* A systolic murmur is present, usually short, low-pitched, coarse, and maximal in the 3d and 4th left interspace close to the sternum, moderately well transmitted to the lungs, but not to the neck. There is a loud, split 2d heart sound frequently followed by an early diastolic murmur in decrescendo. A mid-diastolic rumble at the apex suggests increased flow through the mitral valve. Under the fluoroscope, the ascending aorta is small and quiet, in contrast to the aorta which is observed when a large patent ductus is present. Cardiac catheterization may reveal an increase in oxygen content in the inflow tract of the right ventricle, which serves to differentiate it from a patent ductus, since with the latter one would not expect a rise in oxygen in the inflow tract even with severe pulmonic insufficiency. *More* commonly, the oxygen rise is found in the outflow tract of the right ventricle A further increase in oxygen content may be found in the pulmonary artery because of streamlining of blood from the left ventricle Angiocardiography may be a diagnostic aid Early filling of the left ventricle, but not the left atrium, would indicate shunt from right to left at the ventricular level Reopacification of the right ventricle and pulmonary arteries indicates a left-to-right shunt at the ventricular level However, the surest way of ruling out a patent ductus arteriosus in the infant is the use of retrograde aortography

Large Ventricular Septal Defect with Marked Pulmonary Vascular Disease. This condition is infrequent before the age of 4 but becomes increasingly more common after 10

midline, and if the pulmonary artery is intubated, the origin of the pulmonary artery may be demonstrated in the midline and posteriorly. Unfortunately, it is frequently impossible to catheterize a great vessel. The remaining laboratory findings suggest the presence of a ventricular defect usually of medium or large size

THERAPY. The significant lesion to be treated is the ventricular defect, and the same criteria of management apply to this malformation as to the uncomplicated ventricular defect. No special treatment for the transposition is necessary.

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Tetralogy of Fallot, Large Defect with Severe Pulmonary Stenosis or Pulmonary Atresia (Pseudotruncus Arteriosus). When this combination is present, the major portion of pulmonary blood flow reaches the lungs through collateral vessels arising from the bronchial vessels, the subclavian arteries, the internal mammaries, and occasionally from below the diaphragm. Symptoms are those of extreme fatigability, dyspnea, and cyanosis. In infancy, many patients are subject to repeated spells of *paroxysmal dyspnea*, characterized by a sudden unexplained increase in cyanosis, gasping irregular respirations, a cry of severe pain, and at times, *loss of consciousness*. On physical examination, the cyanosis is marked. A *systolic murmur*, which is high in pitch and moderately long, is heard loudest in the 2d and 3d left interspace Occasionally *no murmur* is present, suggesting either that there is an atresia of the outflow tract of the right ventricle, or that severe polycythemia has increased blood viscosity and decreased the turbulence of blood as it passes through the area of stenosis, therefore making a previously audible murmur inaudible. In the severely cyanotic patient, a careful examination for extracardiac murmurs should be made for, not infrequently, a *soft, continuous humming murmur* will be heard over the back, in the axilla, and to the right and left of the sternum anteriorly. This murmur arises from large tortuous collateral vessels and not from a patent ductus arteriosus Its presence suggests pulmonary atresia. The 2d heart sound at the base of the heart is pure.

imal pulmonary vascular disease, a large left-to-right shunt, and left heart failure

In older patients with moderate or marked pulmonary vascular disease associated with a large or medium-sized ventricular defect, the decision concerning therapy is based on the magnitude and exact nature of the pulmonary vascular changes The principal question to be answered is whether the shunt occurring through the defect is predominantly left to right or right to left. If it is *predominantly left to right*, closure of the defect should result in a drop in pulmonary artery pressure, thus increasing the chances of recovery. A significant drop in pulmonary vascular resistance can be anticipated If, on the other hand, the shunt is *predominantly right to left*, closure of the defect will result in increased pulmonary blood flow against a high vascular resistance, leading to an increase in pulmonary artery pressure and the likelihood of right heart failure If there is clinical or laboratory evidence of left ventricular or left atrial enlargement, the probabilities are that the shunt is still predominantly left to right

Lung biopsies will be of value when more experience in their interpretation is obtained. The presence of marked intimal change and complete occlusion of some arteries with widely patent vessels distally suggests irreversible damage The presence of thick-walled small-lumened vessels with markedly hypertrophied media but little intimal change indicates that the pulmonary vascular disease is probably reversible and correction of the defect can be tolerated.

It should be stressed that therapy for the patient with a large ventricular defect and moderate to severe pulmonary vascular disease cannot be considered comparable to closure of a large patent ductus In the former, it is necessary to approach the defect through the right ventricle A significant portion of right ventricular wall is injured by ventriculotomy, and the efficiency of the right ventricle is temporarily but significantly decreased Surgery should be advised *before* pulmonary vascular resistance has become close to systemic resistance.

Corrected Transposition of the Great Vessels with a Ventricular Septal Defect. In this malformation, the great vessels are transposed, the aorta arising in front and to the left of the pulmonary artery. In addition, the left and right ventricles and the mitral and tricuspid valves are transposed. The left atrium communicates with a ventricle lying to the left, which has the anatomic characteristics of right ventricle and *tricuspid* valve, and communicates in turn with the transposed aorta. The right atrium communicates with a ventricle lying to the right, which has an anatomic *mitral* valve and the characteristics of left ventricle, and communicates with the pulmonary artery lying posterior to the aorta In contrast to the usual form of ventricular defect, in this malformation, the defect opens into the right-sided (or pulmonary) ventricle immediately under the pulmonary valve in the membranous septum and into the left-sided (or systemic) ventricle behind the septal leaflet of the AV valve. Surgical exploration of the right-sided ventricle is made difficult by the anomalous position of the left anterior descending coronary artery which pursues a course directly through the mid-portion of the ventricular outflow tract An anomaly which is frequently associated with corrected transposition and ventricular septal defect is Ebstein's malformation of the left-sided AV valve.

On *fluoroscopy*, the correct diagnosis may be suspected if particular attention is directed to the base of the heart. The left-sided aorta usually alters the left upper configuration of the heart, giving it a straight appearance which extends above the origin of both pulmonary arteries. Electrocardiographic changes relate primarily to the stress placed on one or the other ventricle by the associated ventricular defect. However, varying degrees of AV block including a complete disassociation are common, and their presence should suggest the diagnosis.

Diagnosis of this malformation depends upon the proper evaluation of the origin of the great vessels An angiocardiogram taken in the anteroposterior and the left lateral position will demonstrate that the origin of the aorta is anterior and to the left of the pulmonary artery The right-sided ventricle presents a smooth tract along the inferior margin of the heart toward the apex The left-sided ventricle is not smooth-walled as in the normal individual. The atria are normally positioned During cardiac catheterization, the course of the catheter is more toward the

vere pulmonary stenosis, the main pulmonary artery segment is so small that early complete correction of the defect places an excessive strain on the right side of the heart. On the other hand, creation of a shunt is followed by enlargement of the pulmonary artery, and thus total correction becomes practical at a later date. When complete pulmonary atresia is present, a shunt procedure is the ideal approach. This should be deferred until the child is 3 or 4 years old unless the child's condition is critical. In most instances, a small but patent pulmonary artery to the left or right lung will be found although the main pulmonary artery may be atretic

Tetralogy of Fallot associated with minimal stenosis and a large ventricular defect may be totally corrected using extracorporeal circulation. Since the lungs are protected from progressive pulmonary vascular disease by the infundibular or pulmonary stenosis, surgery can be delayed until the child has reached an adequate size and the risk of correction has been reduced to a minimum For the small defect with marked pulmonary stenosis and minimal or extreme overriding of the aorta, the only surgical approach is complete correction because a shunt procedure too frequently produces cardiac decompensation

Single Ventricle with Pulmonary Stenosis and Minimal or Moderate Pulmonary Vascular Disease. The mitral and tricuspid valves in this malformation open into the common chamber representing both the right and left ventricles The conus area of the right ventricle forms a rudimentary outlet chamber which communicates with the main ventricular chamber through a defect One great vessel arises from the main ventricle, the other from the rudimentary outlet chamber Usually the aorta arises from the anteriorly placed rudimentary outlet chamber, and the pulmonary artery, from the main body of the ventricle in a transposed position. The presence or absence of a transposition of the great vessels, however, has little to do with the clinical course, which is entirely dependent upon the difference in systemic and pulmonary vascular resistances. If pulmonary resistance is low and pulmonary blood flow is high, cyanosis is absent. Despite the fact that there is complete mixing of blood in the common ventricle, the volume of saturated blood returning to the heart is sufficient to raise the saturation of mixed blood above the level where cyanosis is visible.

Differential diagnosis is best made with the laboratory techniques. When the great vessels are transposed, there is a concavity in the region of the main pulmonary artery segment seen both in the PA view and RAO position; yet the lung fields appear excessively vascular. A bulge of the upper left salient of the heart, suggestive of a rudimentary outlet chamber, may be seen. It is usually difficult to be sure which chamber of the heart is enlarged. In one view, the right ventricle may appear enlarged, whereas in another, it is the left ventricle that is enlarged. As a rule, the apex is displaced inferiorly and laterally. The heart presses up against the sternum in the RAO position, but in the LAO position it cuts in anteriorly over the diaphragm, suggesting an absence of the inflow tract of the right ventricle. The ECG of many patients with a single ventricle is extremely bizarre. Not uncommonly an S wave is present in all the standard leads and in chest leads V_1 to V_6. Occasionally, the chest leads pattern may be an R wave throughout. The pattern may be one of pure right or pure left ventricular hypertrophy. In this instance, the findings on fluoroscopy should be taken into account, for it is not uncommon that the chamber which appears enlarged on fluoroscopy will not be the chamber which appeared hypertrophied in the ECG

Angiocardiographic studies may suggest the diagnosis of a single ventricle, particularly if the great vessels are transposed. Filling of the area usually occupied by the left and right ventricle will occur promptly, and in the conus position of the right ventricle, a separately delineated area may be seen, representing the rudimentary outlet chamber. Transposed great vessels in a noncyanotic patient strongly suggest a *single ventricle.* Cardiac catheterization demonstrates a distinct rise in oxygen content on passing through the tricuspid valve. The magnitude of rise demands upon the exact anatomy present, for in certain instances, there may be streamlining of blood so that blood entering the tricuspid valve remains essentially venous until it reaches the outflow tract. A systemic pressure is present within the ventricle. The vessel arising from the main ventricle is usually catheterized without difficulty. Catheterization of the rudimentary out-

Under the fluoroscope, the heart has an accentuated *boot shape* with a marked concavity of the main pulmonary artery segment and an upturned, blunt apex The right and left pulmonary arteries appear small, and the *peripheral lung fields are clear*. When there is severe stenosis associated with an increase in collateral circulation, the markings in both hilar regions may be increased, but the normal vascular pattern is lacking. Angiocardiography fails to demonstrate a main pulmonary artery but may demonstrate filling of the right and left pulmonary arteries from branches arising from the heavily opacified aorta Cardiac catheterization reveals a severe degree of arterial unsaturation The pulmonary artery is only rarely entered because of the severity of the stenosis

Tetralogy of Fallot, Large Defect with Minimal Pulmonary Stenosis. Because the stenosis is minimal in this condition, the shunt is left to right rather than right to left Serial catheterization studies have demonstrated that the stenosis is usually at the level of the crista supraventricularis and may not be significant in early childhood A significant pressure drop appears as cardiac output increases with growth and a hypertrophy of the crista develops The right ventricle is somewhat enlarged because of the increased work load brought about by the pulmonary stenosis. The left ventricle is enlarged because of the increased volume of blood returning from the lungs Clinically, it is difficult to differentiate this condition from a large ventricular defect associated with minimal pulmonary vascular disease *A pulmonary 2d sound that is frequently split but not accentuated suggests infundibular stenosis rather than pulmonary vascular disease* Diastole is usually clear, except for a mid-diastolic rumble at the apex The most useful differential diagnostic tool is cardiac catheterization, provided that the pulmonary artery is entered and the drop in pressure from the main right ventricle to the infundibular area, and through the valve to the pulmonary artery, is demonstrated Pulmonary artery pressure is usually somewhat elevated, but right ventricular pressure is approximately the same as the systemic

Tetralogy of Fallot, Small Defect with Severe Pulmonary Stenosis and No Overriding. The clinical, fluoroscopic, and catheterization findings all are suggestive of isolated valvular pulmonary stenosis with a patent foramen ovale because the resistance to right ventricular outflow is extreme. Angiocardiography offers the best differential diagnosis for a right-to-left shunt occurring at the ventricular level There is early filling of the aorta and a delayed passage of contrast medium through the lungs.

Tetralogy of Fallot, Small Defect with Severe Stenosis and Marked Overriding of the Aorta. In this syndrome, the major work load is placed not on the right ventricle, but upon the left. The right ventricle must meet systemic resistance and, therefore, is moderately hypertrophied. The left ventricle, however, cannot empty efficiently through the tiny ventricular defect. If there is a significant quantity of blood returning to the left side of the heart (as after a Blalock-Taussig or Potts anastomosis), left ventricular enlargement develops, and death from heart failure may occur. The differential diagnosis is extremely difficult. Cardiac catheterization reveals a systemic pressure within the right ventricle and a markedly lowered arterial oxygen saturation The aorta is usually catheterized with ease. A *left-to-right shunt* at the ventricular level may be demonstrated. Angiocardiogram in the LAO projection will reveal early filling of the aorta with delayed filling of the pulmonary vascular tree Late in the series, delayed left ventricular emptying may be demonstrated by retention of the opaque material in the left ventricle.

THERAPY. The therapeutic approach to all these forms of a tetralogy of Fallot is not uniform and depends upon the exact combination of defects The most common form can be improved by creation of a *Blalock-Taussig subclavian–pulmonary artery anastomosis* or by a *Potts aortic-pulmonary anastomosis* In more recent years, the defect has been completely repaired by closure of the defect and resection of the infundibular or valvular stenosis while using an *extracorporeal circulation*. When a patient with a tetralogy of Fallot is not severely incapacitated, corrective surgery should be withheld until the child is 4 years or older. On the other hand, infants suffering from attacks of paroxysmal dyspnea should have an anastomosis. This is a safer procedure in infancy and permits growth and development to the point where complete correction is possible. It is also probable that, in cases of se-

that of *left axis deviation* and *left ventricular hypertrophy*. Cardiac catheterization is of little aid, for in many instances the only chamber that can be catheterized is the right atrium. The catheter may slip through the atrial defect into the left atrium and ventricle, but it is rare to catheterize either great vessel. The findings are a rise in oxygen content at the ventricular level, with a saturation that is identical to that determined from the brachial artery. Ventricular pressure is systemic. Arterial unsaturation is present. Angiocardiography in the LAO view may be of assistance in demonstrating prompt filling of the left atrium from the right and a large and thick-walled left ventricle, with filling of the pulmonary artery and aorta from the common left ventricle. In the LAO position, that portion of the heart lying anteriorly and immediately over the diaphragm, which is usually occupied by the inflow tract of the right ventricle, does not fill with contrast medium.

THERAPY. A corrective therapeutic procedure for tricuspid atresia has not been developed. Consequently, the approach is palliative and consists of an anastomosis between the pulmonary artery and a systemic artery The mortality rate during and after surgery is significantly higher than for tetralogy of Fallot. If there is evidence of obstruction between the atria at the time the anastomosis is created, the atrial defect should be enlarged Surgery for this malformation is best carried out after the age of 2 since operation before then is attended by a greater mortality rate However, if the patient has episodes of paroxysmal dyspnea, surgery should not be withheld.

Tricuspid Atresia with Transposition of the Great Vessels. This rare malformation places a severe load upon the pulmonary vascular bed, and if the patient survives the first year, the degree of pulmonary vascular disease is usually marked. A high pulmonary resistance must be maintained in order to balance, not only the normally elevated systemic resistance, but also the additional resistance to aortic flow created by the small ventricular defect and rudimentary right ventricle from which the aorta arises. In early infancy, signs and symptoms are those of a single ventricle with a high pulmonary blood flow. However, the rapid progression of the pulmonary vascular disease decreases pulmonary blood flow, so that the signs and symptoms become those of a single ventricle with pulmonary stenosis or marked pulmonary vascular disease.

Differential diagnosis depends upon the laboratory studies. Fluoroscopy reveals increased vascular markings without fullness of the main pulmonary artery segment. The heart is usually enlarged, and the enlargement involves the right atrium, the left ventricle, and during early infancy, the left atrium The contour of the heart may suggest a tricuspid atresia. The ECG reveals left ventricular hypertrophy. Cardiac catheterization is of little aid. Angiocardiography demonstrates the presence of tricuspid atresia and the transposed position of the great vessels.

THERAPY. Theoretically, the therapeutic approach should aim to relieve the resistance to aortic outflow and increase pulmonary artery resistance. Thus, to widen the ventricular septal defect and to create pulmonary stenosis would appear to be the procedure of choice Correction of the transposition is of doubtful value since the coronary arteries would continue to arise from the obstructed vessel.

Transposition of the Great Vessels with Patent Ductus Arteriosus or Ventricular Septal Defect. Transposition of the great vessels has been included in group I because there is a definite relationship between alterations in the pulmonary vascular bed, size of defect, presence or absence of pulmonary stenosis, and clinical course, despite the separation of the two circulations into two independent units A large ventricular defect or large patent ductus combined with a transposition leads to the rapid development of pulmonary vascular disease The speed of development is enhanced by the polycythemia and perhaps by pulmonary vascular spasm induced by anoxemia

In this malformation, the great vessels are transposed, the aorta arising from the right ventricle and the pulmonary artery from the left Since venous return to the heart is normal, two potentially completely independent circulations exist Venous blood returning from the body is directed through the aorta back to the body, and oxygenated blood returning from the lungs is redirected to the lungs In the absence of any communication between the two circulations, this malformation would be incompatible with life However, if one or

let chamber and remaining great vessel is rarely accomplished

THERAPY. At the present time, corrective surgery is not available. The only procedure that offers improvement is the production of pulmonary stenosis by banding the pulmonary artery to reduce its lumen size by approximately 75 per cent before pulmonary vascular disease has developed to the irreversible stage It is best accomplished when the pulmonary blood flow is high, for determinations of pressure proximal and distal to the area of stenosis indicate whether sufficient stenosis has been created. The distal systolic pulmonary artery pressure should be lowered to 30 to 40 mm Hg When flows are equal preoperatively, a pressure drop in the distal pulmonary artery indicates excessive stenosis, consequently, the pulmonary artery must be narrowed to a degree just a fraction less than that which will produce a pressure drop

Single Ventricle with Pulmonary Stenosis. In this malformation, the pulmonary stenosis is usually due to a pulmonary valve ring which is narrowed, sclerosed, and surrounded by thickened, fibrous endocardium Signs and symptoms vary according to the degree of pulmonary stenosis. The great vessels are usually transposed. The importance of differentiating the single ventricle with pulmonary stenosis from the teralogy of Fallot is that complete correction of the latter is practical, whereas it is *not* with a single ventricle. Differential diagnosis is also important because surgery of the single ventricle with pulmonary stenosis is attended by a higher mortality rate (25 per cent) than is the same palliative therapy for tetralogy of Fallot The correct differential diagnosis is dependent upon a high level of suspicion, with attention paid to the slightest variation from the typical tetralogy of Fallot. Under the fluoroscope, the heart frequently has the contour of a tricuspid atresia In the PA projection, the heart appears fat, and the apex extends below the diaphragm, failing to clear even on deep inspiration In the LAO position it may cut in sharply over the diaphragm anteriorly When the great vessels are transposed, the area usually occupied by the main pulmonary artery is occupied by the aorta; consequently, there is no concavity. The ECG usually differs from that found in tetralogy of Fallot in that it does not have a pure pattern of right ventricular hypertrophy. Cardiac catheterization, unless both great vessels are catheterized and their origin is determined, is of little differential diagnostic aid. Angiocardiography is of help since both right and left ventricular areas are filled simultaneously, and the exact origin of the great vessels may be clarified.

THERAPY. Therapy is, of necessity, palliative since total correction of the defect is not yet possible. An anastomosis between a systemic artery and the pulmonary artery should be created It is important that the shunt not be too large because, in this malformation, there is a high instance of congestive failure postoperatively.

Tricuspid Atresia. In this malformation, the tricuspid valve is atretic and is represented by a small dimple in the wall of the right atrium. There is no continuity of right atrium and right ventricle The inflow tract of the right ventricle does not develop. Blood returning to the right side of the heart must pass through an atrial defect into the left atrium and left ventricle. From the left ventricle, blood may pass out of the aorta or through a ventricular defect into a rudimentary right ventricle, which communicates with the pulmonary artery. In most instances, the ventricular defect is relatively small and the rudimentary right ventricle is long and narrow, offering a significant resistance to pulmonary blood flow. Signs and symptoms are comparable to a tetralogy of Fallot and depend upon the degree of pulmonary obstruction. In addition, however, a small atrial defect may hinder the free flow of blood from right atrium to left atrium, causing an increased systemic venous pressure.

Fluoroscopic examination reveals a boot-shaped heart, which appears much thicker than is usual with the tetralogy of Fallot There is a rounding and fullness of the left upper salient of the heart both in the PA projection and in the RAO view, which represents rudimentary right ventricle The apex does not clear the diaphragm, and in the LAO view, there is a posterior rounding suggestive of left ventricular enlargement. The right atrium, usually normal in size in the tetralogy, not infrequently is enlarged The left atrium is normal. The ECG presents the best differential diagnostic information The pattern is

ventricular defect, the functional size of the latter is made larger, thus permitting a far larger bidirectional shunt. Arterial oxygen saturation is higher and cardiac failure less common, so that this diagnosis should be suspected in any patient with a transposition living past the tenth year. The cause of death is usually related to severe pulmonary vascular disease and anoxia.

The differential diagnostic points, aside from the age of the patient, are chiefly associated with laboratory studies. X-ray and fluoroscopy reveal a fullness of the main pulmonary artery segment as visualized in the PA view, which is not often present in other forms of transposition of the great vessels The hilar markings are increased. On angiocardiography, there is simultaneous filling of both the anteriorly placed aorta and the posteriorly placed pulmonary artery. The volume of contrast medium is greater in the aorta. During cardiac catheterization, it is usually possible to enter both the pulmonary artery and aorta and to demonstrate an increase in oxygen content in the pulmonary artery over that obtained high in the outflow tract of the right ventricle. Right ventricular and left ventricular pressures are equal. Determination of pulmonary vascular resistance indicates the presence of marked pulmonary vascular disease

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Transposition of the Great Vessels with Ventricular Septal Defect and Pulmonary Stenosis. The presence of pulmonary stenosis effectively reduces pulmonary blood flow, which decreases the likelihood of congestive failure and causes a left-to-right shunt at the ventricular level. The degree of cyanosis depends upon the severity of the pulmonary stenosis and the magnitude of the bronchial arterial circulation. On physical examination, a high-pitched, long systolic murmur is usually present at the base of the heart, which suggests a pressure gradient across the pulmonary valve. There is no evidence of congestive failure. The pulmonary 2d sound is usually pure but *may be loud*, since it is caused by closure of the anteriorly placed aortic valve. On x-ray, the peripheral lung fields appear clear and not pulsatile, and the main pulmonary artery segment is concave. The heart is not grossly enlarged and tends to lie in a more horizontal plane rather than at a 45° angle. Evidence of left ventricular and left atrial enlargement is usually absent because of the reduction in the volume of blood returned to the left side of the heart. The ECG reveals *right axis deviation* and *pure right ventricular hypertrophy*. A misdiagnosis of tetralogy of Fallot is frequently made Angiocardiography may establish the diagnosis if there is opacification of the pulmonary artery late in the series However, as a rule, the only vessel to opacify is the aorta, the anterior origin of which may be suspected but not proved In a few patients with this malformation, the aorta arises far to the left and produces a convexity in the usual position of the pulmonary artery. When this area is seen to fill with contrast solution and is defined as aorta, the diagnosis becomes clear. Cardiac catheterization is of little aid.

THERAPY FOR TRANSPOSITION OF GREAT VESSELS Corrective surgery for this malformation is still experimental There are several palliative procedures which may improve exercise tolerance and prolong life expectancy. The creation of an atrial septal defect increases bidirectional shunting The transplantation of the right pulmonary veins to the right atrium accomplishes essentially the same physiologic change. Transposition of the inferior vena cava and right pulmonary veins still further improves systemic saturation However, none of these procedures prevents the progressive development of pulmonary vascular disease, and none establishes a circulation sufficiently adequate to give a normal life expectancy.

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more defects are present, a bidirectional shunt is established and oxygenated blood may reach the body. There is no stress on the circulation during intrauterine life. It is only following birth, when the newborn infant has become dependent upon the lungs for adequate gaseous exchange, that stress appears. Thus, the heart is of normal size at birth, but enlarges rapidly during the early months of life. Cyanosis is severe, and cardiac decompensation usually appears during the first year of life.

The incidence of failure appears to bear an inverse relationship to the size of the defect for the following reasons: patients with cyanotic heart disease develop an increased bronchial flow with an increase in size of the anastomotic channels between the pulmonary arterial bed and the bronchial vessels. Thus, in transposition of the great vessels, blood is continually drained from the aorta, entering the lungs through bronchial vessels and eventually returning to the left atrium and not the systemic circulation. If the defect connecting the two circulations is small, the volume of blood recirculating through the lungs steadily increases until failure of the left side of the heart occurs. The reason for failure of the right side of the heart is less clear but may be related to myocardial hypoxia and the increased work load placed on the right side by having to pump a highly viscid form of blood.

Transposition of the Great Vessels with Small Patent Ductus Arteriosus and Patent Foramen Ovale. Cyanosis is early and intense. Cardiac failure generally appears within the first few weeks of life, and the life expectancy is under 1 year. Differential diagnosis is usually not difficult, except during the first week of life. The presence of intense cyanosis associated with evidence of biventricular enlargement and cardiac failure is strong presumptive evidence. Differential cyanosis may be present if the direction of shunt through the patent ductus arteriosus is from pulmonary artery to aorta, for the oxygen content of blood in the descending aorta is higher than in the ascending aorta.

On physical examination, the baby appears acutely ill, with rapid respirations and intense cyanosis. Peripheral pulses may be normal. The heart is enlarged, the apex is frequently in the 5th left interspace in the anterior axillary line. Murmurs are usually absent. The 2d heart sound at the base is accentuated and usually split. Rales are frequently heard over the lungs, and there is evidence of increased systemic venous pressure, with enlargement of the liver and a thick skin. On x-ray and fluoroscopy, the earliest differential diagnostic point is the axis of the heart. Instead of lying transversely, the *long axis of the heart is at a 45° angle, suggesting equal enlargement of both the left and right ventricle.* The main pulmonary artery segment is concave. The peripheral lung fields appear vascular and pulsatile. The ECG reveals a normal neonatal pattern, except for increased amplitude in the chest leads. The angiocardiogram reveals early filling of the aorta which, in the oblique views, lies anteriorly. It is unusual to see contrast solution in the lungs. Cardiac catheterization is of little diagnostic aid.

Transposition of the Great Vessels with Large Ventricular Septal Defect and Moderate to Severe Pulmonary Vascular Disease. This combination is more compatible with life than that just discussed. Failure appears late, if at all, and the cause of death is usually anoxia rather than cardiac decompensation. Cyanosis is usually intense. The physical findings are similar to those of a transposition and a small patent ductus, except for the absence of cardiac failure and the presence of a murmur at the base of the heart. The most likely associated anomaly is a large ventricular septal defect. X-ray reveals a heart with its long axis at a 45° angle, a concave main pulmonary artery segment, vascular lung fields, and enlargement of all chambers. Angiocardiography reveals the anterior origin of the aorta and may suggest a right-to-left shunt at the ventricular level, with some opacification of the posteriorly placed pulmonary artery. Cardiac catheterization reveals the presence of a left-to-right shunt at the ventricular level, a common systolic pressure within both ventricles, and when the aorta is entered, confirmation of the anterior origin of the aorta.

Transposition of the Great Vessels with Large Ventricular Septal Defect, Overriding Pulmonary Artery, and Moderate to Severe Pulmonary Vascular Disease (Taussig-Bing Syndrome). In this malformation, the pulmonary artery is not completely transposed but overrides a ventricular defect. Because of the origin of the pulmonary artery just above the

ventricular defect, the functional size of the latter is made larger, thus permitting a far larger bidirectional shunt. Arterial oxygen saturation is higher and cardiac failure less common, so that this diagnosis should be suspected in any patient with a transposition living past the tenth year The cause of death is usually related to severe pulmonary vascular disease and anoxia

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septum, which directs caval return through the mitral valve and pulmonary venous return through the tricuspid valve This procedure appears technically feasible when using extracorporeal circulation However, it must be done at an early age, before pulmonary vascular disease has developed to an excessive degree, which adds to the procedure the major complication of infancy and small patient size.

Defects between the Ventricles or Great Vessels with Obstruction of the Pulmonary Venous Return. In contrast to the malformations which have been discussed so far, damage occurs to the lungs in utero when obstruction of the pulmonary venous return is present prior to birth Such obstruction may consist of anomalies of the pulmonary veins, mitral atresia associated with a closed or small foramen ovale and a *cor triauriculare* Damage *in utero occurs* because the major resistance to pulmonary blood is venous and not arterial, this leads to dilatation and hypertrophy of the capillaries, thickening of the alveolar wall, and the deposition of hyaline material and cellular infiltrate between the capillary and alveolar walls Thus, gaseous exchange after birth is hindered by a diffusion problem In addition, the lowered pulmonary arteriolar resistance transmits a greater load from the pulmonary arterial bed to the obstructed venous return, and pulmonary vascular disease develops rapidly Consequently, when a defect between the great vessels or ventricles is associated with pulmonary venous obstruction, the symptomatology, course, and prognosis for survival are much worse Pulmonary vascular disease is intense, and as a rule the patient does not pass through the phase of high output cardiac failure, but passes directly to the phase of right-to-left shunt with severe hypoxia associated with attacks of paroxysmal dyspnea and early death The increase in magnitude of pulmonary vascular disease is attested to by the lumen-wall ratio

Aortic and Mitral Atresia with Patent Ductus Arteriosus and Small Patent Foramen Ovale. In this malformation, since the mitral valve is atretic, the left ventricle forms a small blind sac or communicates with the right ventricle through a small ventricular defect The total cardiac output passes through the pulmonary artery, with some blood reaching the lungs but the major portion passing through a large patent ductus into the aorta, because of the high pulmonary vascular resistance. The aorta, proximal to the origin of the ductus, becomes progressively smaller, so that the ascending aorta is tiny and ends in an atretic aortic valve and the two coronary arteries The left atrium and pulmonary veins are abnormally small Since the valve of the foramen ovale lies on the left atrial side, any increase in pressure in the left atrium without other avenues of egress tends to close the valve, making it more difficult for blood returning from the lungs to reach the systemic circulation. Thus pulmonary venous obstruction leads to the production of early alveolar wall thickening and capillary damage Resistance to pulmonary blood flow is high at the time of birth and remains high The heart tends to be abnormally large at the time of birth, for reasons probably associated with inadequate coronary blood flow, and enlarges very rapidly in the newborn period Hypoxia is extreme, and death generally occurs during the first week of life, not only because of the high pulmonary resistance, but also because of the diffusion difficulty resulting from the thickened capillary and alveolar wall

Aortic atresia should be suspected in the child who is intensely cyanotic in the first hours of life. The peripheral pulses are weak, and the heart is enlarged Murmurs are usually absent. The 2d heart sound is pure There is evidence of systemic venous congestion, but the lungs are clear. The ECG reveals right ventricular hypertrophy On fluoroscopy, the heart is large because of enlargement of the right ventricle, right atrium, and a convex main pulmonary artery segment The peripheral lung fields are clear

It is essential to distinguish this malformation from isolated valvular pulmonary stenosis, since pulmonary stenosis can be cured surgically and aortic atresia cannot The findings may be similar. In this condition, however, a systolic murmur over the base of the heart is seldom heard, whereas with extreme valvular pulmonary stenosis and a patent foramen ovale, a murmur is usually present. In aortic atresia, the right ventricle, pulmonary artery, and descending aorta are rapidly visualized with contrast medium, but the ascending aorta

and the right and left pulmonary arteries are small.

At the present time, there is no therapy.

Mitral Atresia with Ventricular Septal Defect and Patent Foramen Ovale. In contrast to the malformation just discussed, some of the blood reaching the aorta passes through a ventricular septal defect and into the ascending aorta. The major portion, however, reaches the aorta through a ductus arteriosus. The clinical manifestations, course, and prognosis are similar to those of aortic atresia plus mitral atresia.

Congenital Mitral Stenosis with a Patent Ductus Arteriosus. In this malformation, the primary lesion is severe mitral stenosis caused by an abnormally small valve ring and a thickened, abnormally formed mitral valve with shortened chordae tendineae, and frequently with adhesions of part of the valve leaflet to the wall of the ventricle Pulmonary venous and capillary changes occur prior to birth because of the mitral obstruction, and a markedly elevated pulmonary resistance remains after birth. The clinical findings are those of a large patent ductus arteriosus associated with severe pulmonary vascular disease. *Cyanosis* is usually present early, and *differential cyanosis* between the upper and lower extremities may be noted.

The correct diagnosis of this malformation depends upon recognition of the mitral stenosis, which is suggested by the presence of a long diastolic rumble at the apex Frequently, there is a systolic murmur indicative of some degree of mitral insufficiency. Marked enlargement of the left atrium may be noted on fluoroscopy. The ECG shows a *notched P wave* in the limb leads and a *large P wave* with a *short P-R interval* over the left precordial leads, indicative of left atrial hypertrophy. Angiocardiography confirms the presence of a large left atrium and usually demonstrates the presence of a patent ductus arteriosus, a high pulmonary artery pressure, and marked elevation of the pulmonary wedge pressure.

THERAPY. *Closure of the ductus* should be of benefit unless the shunt is predominantly right to left. If possible, *dilatation of the mitral valve* should be attempted, but since the usual form of congenital mitral stenosis consists of a very small mitral ring, correction of the stenosis is extremely difficult. In the presence of a predominant right-to-left shunt, a two-staged surgical approach should be tried The mitral stenosis should be corrected. Sufficient time should then be allowed for a decrease in pulmonary resistance, and then an attempt should be made to close the patent ductus arteriosus.

Congenital Mitral Stenosis with a Ventricular Septal Defect. In this malformation, the predominant lesion again is mitral stenosis. The findings are those of a ventricular septal defect with moderate to marked pulmonary vascular disease and with mitral stenosis When the shunt is predominantly left to right, the surgical approach is *closure of the defect* and *resection of the stenosis* under direct vision, using extracorporeal circulation. If the shunt is predominantly right to left, the mitral stenosis should be relieved first, thus permitting a drop in pulmonary resistance, at a later date, attempts can be made to close the defect

GROUP II: DEFECTS BETWEEN THE ATRIA

The direction and volume of shunt depend upon the relative filling pressure of the right and left ventricles. Normally, the tricuspid orifice is larger than the mitral and the inflow tract of the right ventricle is wider than that of the left After birth, the difference between pulmonary and systemic vascular resistance leads to progressive thickening of the left ventrical and thinning of the right Because of these differences, it takes less pressure to fill the right ventricle, and the normal left atrial pressure is significantly greater than the right When the two atria communicate through a large defect, an essentially uniform pressure exists, which is lower than the normal left atrial pressure and higher than the right. A left-to-right shunt develops, the stroke volume of the right ventricle is greater than the left, and the size of the right ventricular chamber increases Increased chamber size leads to decreased filling pressure, an increased shunt, and further dilatation of the right ventricle It is only when the right ventricle fails to empty that filling pressure rises; then the shunt is decreased and, perhaps, reversed.

Since the right and left ventricles are essentially the same size at birth, the left-to-right shunt is small Pulmonary resistance falls, and the fetal pulmonary vascular pattern is not

septum, which directs caval return through the mitral valve and pulmonary venous return through the tricuspid valve. This procedure appears technically feasible when using extracorporeal circulation. However, it must be done at an early age, before pulmonary vascular disease has developed to an excessive degree, which adds to the procedure the major complication of infancy and small patient size.

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Aortic and Mitral Atresia with Patent Ductus Arteriosus and Small Patent Foramen Ovale. In this malformation, since the mitral valve is atretic, the left ventricle forms a small blind sac or communicates with the right ventricle through a small ventricular defect The total cardiac output passes through the pulmonary artery, with some blood reaching the lungs but the major portion passing through a large patent ductus into the aorta, because of the high pulmonary vascular resistance The aorta, proximal to the origin of the ductus, becomes progressively smaller, so that the ascending aorta is tiny and ends in an atretic aortic valve and the two coronary arteries The left atrium and pulmonary veins are abnormally small. Since the valve of the foramen ovale lies on the left atrial side, any increase in pressure in the left atrium without other avenues of egress tends *to close the* valve, making *it more difficult for blood returning from the lungs to reach the systemic circulation. This* pulmonary venous obstruction leads to the production of early alveolar wall thickening and capillary damage Resistance to pulmonary blood flow *is high* at the time of birth and *remains high. The heart* tends to be abnormally large *at the time of* birth, for reasons probably associated with inadequate coronary blood flow, and enlarges *very rapidly in the newborn period. Hypoxia is extreme,* and death generally occurs during the first week of life, not only because of the high pulmonary resistance, but also because *of the diffusion* difficulty resulting from the thickened capillary and alveolar wall.

Aortic atresia should be suspected in the child who is intensely cyanotic *in the first* hours of life. The peripheral pulses are weak, and the heart *is enlarged.* Murmurs are usually absent The 2d heart sound is pure. There *is evidence of* systemic venous congestion, but the lungs are clear The ECG reveals right ventricular hypertrophy On fluoroscopy, the heart is large because of enlargement of the right ventricle, right atrium, and a convex *main* pulmonary artery segment The peripheral lung fields are clear

It is essential to distinguish this malformation from isolated valvular pulmonary stenosis, since pulmonary stenosis can be cured surgically and aortic atresia cannot. The findings may be similar. In this condition, however, a systolic murmur over the base of the heart is seldom heard, whereas with extreme valvular pulmonary stenosis and a patent foramen ovale, a murmur is usually present. In aortic atresia, the right ventricle, pulmonary artery, and descending aorta are rapidly visualized with contrast medium, but the ascending aorta

to the axilla. The *2d sound at the base is split* and usually somewhat accentuated. In some patients, a decrescendo murmur of pulmonic insufficiency may be heard along the left sternal border. Except when the right ventricle has failed, the lungs are clear, hepatic enlargement is not present, and there is no peripheral edema.

The peripheral pulmonary vascular markings are increased and actively pulsatile, and the primary vessels are convex, dilated, and pulsating. Evidence of right ventricular enlargement is present in the lateral displacement of the apex, and a decrease in the retrosternal space is noted in the RAO view. The aorta is small, the left ventricle and atrium are normal in size. The ECG presents the pattern of an *incomplete right bundle branch block* with *diastolic overload of the right ventricle,* characterized by an RSR' pattern in the right precordial leads. An angiocardiogram demonstrates a large pulmonary artery and large right ventricle and atrium, which reopacify early in the series Flow through the lungs is rapid. If cinefluorography is used, there may be intermittent opacification of the left atrium when visualized in the LAO view It is frequently possible to catheterize both the left atrium and left ventricle, in addition to demonstrating a left-to-right shunt at the atrial level. A pressure gradient across the pulmonary valve may be present, depending upon the degree of "relative stenosis," and may be expected to disappear following closure of the defect.

THERAPY. Surgical closure of the septum secundum defect has been sufficiently developed and may be warranted for any young person over the age of 10 years with evidence of right ventricular enlargement, even in the absence of symptoms, because the likelihood of irreversible pulmonary vascular disease at an older age is very great The methods of closure are varied and too numerous to be detailed here.

Septum Secundum Defect with Minimal Pulmonary Vascular Disease and Partial Anomaly of the Pulmonary Venous Return. In this malformation, one or more of the pulmonary veins may enter the right atrium either directly or via the superior or inferior vena cava or the coronary sinus As a consequence, the left-to-right shunt is larger in the newborn period; signs, symptoms, and pulmonary vascular disease are more likely to develop at an earlier age, particularly if more than one pulmonary vein enters the atrium The clinical findings cannot be differentiated from those of a simple secundum defect. The differential diagnosis rests upon accurate cardiac catheterization and dye-dilution studies. The differential injection of dye into the right and left pulmonary arteries separately may indicate the location of an anomalous vein.

THERAPY. The presence of an anomalous pulmonary vein increases the need for surgical correction. When closing an atrial septal defect, the surgeon should always inspect for an anomalous vein and, if present, should divert it into the left atrium.

Septum Secundum Defect with Mild to Moderate Pulmonary Stenosis. In this malformation, the direction and volume of shunt depend upon the severity of the pulmonary stenosis. When the *stenosis is mild,* the shunt is from left to right, and symptoms are comparable to those of a simple secundum defect When the *stenosis is moderate,* the volume of shunt is decreased since right ventricular filling pressure is increased. There may be periods of right ventricular failure when increased cardiac output is necessitated by *exercise* or pulmonary resistance is further elevated by a concomitant *pulmonary infection.* Dyspnea is severe with exercise, and cyanosis may be apparent On examination, the *systolic murmur* at the base of the heart is loud, long, and often high-pitched, without the characteristics which are usually associated with a simple septum secundum defect The ECG may give evidence of both *systolic and diastolic overload* of the right ventricle. A pressure gradient drop across the pulmonary valve is present which, if minimal and accompanied by a large left-to-right shunt, will disappear following closure of the defect. If the pressure differential is below 50 mm Hg and the shunt is large, surgical closure reestablishes a normal pressure relationship However, if the pressure gradient is over 50 mm Hg and the shunt is small, the stenosis is truly significant and should be corrected. Consequently, before deciding whether to perform a pulmonary valvulotomy, right ventricular and pulmonary artery pressures should be obtained at the time of surgery both before and after closure of the defect.

maintained Pulmonary pressure becomes elevated only after the total pulmonary vascular bed has been utilized, either because of the magnitude of the shunt or the reduction in lung mass caused by repeated parenchymal infection Elevated pulmonary pressure ultimately leads to *pulmonary vascular disease*, which is characterized by *predominant intimal proliferation* in contrast to the predominant medial hypertrophy accompanying the large ventricular defect. The rapidity with which pulmonary vascular disease develops is extremely variable Once it has started, however, it tends to progress with increasing momentum.

Since the chamber size and filling pressure of the right ventricle (rather than the resistance offered by the defect itself) control the volume of shunt, the clinical manifestations cannot be discussed in terms of a large, medium, or small defect An exception to this is the *patent foramen ovale associated with Ebstein's malformation of the tricuspid valve or with severe right ventricular outflow obstruction;* then, the foramen is functionally patent only when the right atrial pressure exceeds the left. Consequently, the factors which alter the clinical syndrome presented by a patient with an atrial defect relate to the degree of pulmonary stenosis or the magnitude of pulmonary vascular disease and to the age of the patient when a high flow develops A *small shunt after birth* permits normal disuse atrophy of the pulmonary vessels and a normal low pulmonary vascular resistance A *large shunt after birth* utilizes the total pulmonary vascular bed and leads to the retention of the fetal pulmonary vascular bed Therefore, the discussion of this group of malformations should be broken down according to the stage of development in which stress becomes significant and the pressure and degree of pulmonary stenosis or pulmonary vascular disease Therefore, comprehensive grouping is not so applicable as with the malformation listed in group I.

Septum Secundum Defect with Minimal Pulmonary Vascular Disease. In this relatively common malformation the *atrial defect* involves that portion of septum which is clearly above the AV valves and *usually* contains the foramen ovale It rarely causes severe symptoms in early childhood, for symptoms are absent until the volume of shunt has achieved significant proportions. The date of onset of symptoms is extremely variable, which may be related to (1) the changes in the total available pulmonary vascular bed brought about by recurrent infections or structural pulmonary disease, (2) the structural differences in the right ventricle permitting a lower filling pressure in certain individuals, (3) the susceptibility and rapidity of response of the pulmonary vascular bed to the elevated flow. Rapidly progressive pulmonary vascular disease occurs most frequently during the *late teens.* It is rather common to see a patient, who is free of symptoms and has only a minimal increase in pulmonary resistance, develop in a matter of months a *right-to-left shunt* and such extensive irreversible pulmonary vascular damage that surgical correction is impossible

It is usual to see *left atrial enlargement*, despite the large return of blood to that chamber, for the wall of the left atrium is more muscular and less distensible than that of the right. *When the heart fails*, the venous pressure is elevated *not only* in the systemic circulation, but in the pulmonary circulation as well, causing symptoms of systemic and pulmonary congestion It is probable that both ventricles *fail, though for different* reasons.

Signs and symptoms are related to the volume of shunt and the efficiency of the right ventricle. *Exertional dyspnea* and *impaired growth and development* are common, because of a high incidence of pulmonary infection, pulmonary congestion, and perhaps also a reduced systemic blood flow. Right heart failure causes *severe exertional dyspnea, peripheral edema, orthopnea, and pulmonary congestion* Peripheral pulses are normal. A *bulge of the precordium*, increased precordial activity, and an impulse close to the sternum, which is strikingly more forceful than that at the apex, suggest that the right ventricle alone is under stress. The apical thrust is displaced laterally. A *systolic murmur*, probably caused by relative pulmonary stenosis, is usually heard over the base of the heart. It is short, early in timing, moderately loud, and transmitted over the lungs. A *mid-diastolic rumble* is frequently heard just medial to the apex, in contrast to the murmur of *mitral stenosis*, it is better transmitted toward the sternum than outward

may be demonstrated by catheterization. Careful pullback pressure tracings from the pulmonary artery into the right ventricle usually should isolate the area of stenosis to the valve ring. Arterial unsaturation is present.

THERAPY. The best approach, except in the tiny infant, appears to be direct visualization of the pulmonary valve through the open pulmonary artery during inflow occlusion, using either *hypothermia* or *extracorporeal circulation*. In adults, who have developed sufficient hypertrophy and scarring of the ventricular outflow tract to cause further obstruction, extracorporeal circulation should probably be used in order to gain sufficient time to correct the additional stenosis The blind approach to the pulmonary valve through the right ventricle in the small infant still appears safer and adequate, since there is much less right ventricular hypertrophy and the pulmonary valve itself is thin, easily torn, and less liable to stretch. However, the efficacy of valvulotomy should be determined by preoperative and postoperative pressure tracings, and if adequate relief of stenosis has not been achieved, a second attempt should be made

Patent Foramen Ovale with Infundibular Pulmonary Stenosis. In this malformation, the area of stenosis is located proximal to the pulmonary valve, in the infundibular portion of right ventricle The signs and symptoms closely simulate those of isolated valvular pulmonary stenosis and patent foramen ovale, except for the position and spread of the *systolic murmur* which is usually *high-pitched, long, and heard best in the 3d left interspace,* not well transmitted toward the left clavicle. A split soft 2d sound may be present, and diastole is clear. On fluoroscopy, in contrast to valvular stenosis, the main pulmonary artery segment is *not* convex in the PA and RAO views, and there is no enlargement of the major branches The angiocardiogram may indicate that the stenosis lies proximal to the pulmonary valve and is separated from the pulmonary valve by an infundibular chamber. Catheterization with slow pullback maneuvers from the pulmonary artery into the right ventricle should indicate the point of stenosis. In the infundibular chamber, the systolic pressure is equal to that of the main pulmonary artery, but the diastolic pressure approaches zero.

THERAPY. Corrective surgery consists of excision of the stenotic area under direct vision, using inflow occlusion with either *extracorporeal circulation* or *hypothermia*. The former seems preferable because of the length of time it may take to perform an adequate resection. The area of stenosis may be approached from either the right ventricular wall or the pulmonary artery.

Patent Foramen Ovale with Severe Pulmonary Vascular Disease. In this condition, the primary disease process is in the pulmonary vascular bed Sufficient elevation of pulmonary resistance occurs to produce marked right ventricular hypertrophy, an increase in filling pressure of the right ventricle,[9] and a right-to-left shunt through the probe-patent foramen ovale The etiology of the disease is not understood, although there is some evidence to suggest a neurogenic origin The early morphologic changes are primarily *medial hypertrophy* of the small pulmonary vessels and *small areas of acute pulmonary arteritis*. Thickening of the veins is also present. The terminal picture is one of severe pulmonary artery obstruction with marked intimal proliferation, destruction of the media with replacement by fibrous tissue, and suggestive evidence of *thrombus* formation. Distal to the point of obstruction, thin-walled dilated pulmonary vessels may be seen. The age of onset of symptoms is highly variable.

The symptoms suggest valvular pulmonary stenosis *Cyanosis* and *dyspnea* are severe Right heart failure is progressive and eventually leads to death. On physical examination, the right ventricle is found to be enlarged and evidence of failure may be present. A *short* basal systolic murmur may be present The 2d sound at the base of the heart is *accentuated* and *split*. A long *decrescendo diastolic blowing murmur* along the left sternal border suggests *pulmonary insufficiency*. The ECG reveals a *systolic overload* of the right ventricle and a *tall peaked P wave* suggestive of right atrial hypertrophy. The x-ray and fluoroscopy picture frequently resembles that of isolated valvular pulmonary stenosis In a few instances, however, there may be increased peripheral pulmonary markings, sug-

[9] See note 6 *Editor.*

Septum Secundum Defect with Severe Pulmonary Stenosis. In this malformation, the severity of the pulmonary stenosis produces a decreased pulmonary blood flow, an increased filling pressure of the right ventricle[6] (greater than that of the left ventricle), and a predominant right-to-left shunt through the atrial defect. Cyanosis, severe exertional dyspnea, and orthopnea[7] are occasionally seen. The *systolic murmur at the base* of the heart is high-pitched, long, loud, well transmitted upward, toward the left clavicle, and is accompanied by a thrill The pulmonary 2d sound is pure and soft Presystolic pulsations of the liver may be present A decrescendo murmur of pulmonary insufficiency is not present nor is the mid-diastolic rumble of relative tricuspid stenosis The right ventricle and right atrium are seen enlarged on fluoroscopy and the main pulmonary artery is full and pulsatile, but in contrast to this, the pulmonary stems are less pulsatile and the peripheral lung fields are clear and show no pulsations.

There is evidence in the ECG of both *systolic and diastolic overload* of the right ventricle, characterized by an RSR' pattern in the right precordial leads, associated with a tall R and a deep S over the left precordial leads T wave changes suggestive of right strain are present Cardiac catheterization helps to differentiate this defect from isolated valvular pulmonary stenosis with patent foramen ovale, for in the latter, there is evidence of a small left-to-right shunt With cinefluorography, the bidirectional shunt through the atrial septum may outline the defect, and the exact site of the stenosis may be localized

THERAPY The importance of the differentiation between valvular pulmonary stenosis associated with large atrial defect and one with a patent foramen ovale is in the surgical correction Resection of the area of stenosis when the atrial defect is large will produce a large left-to-right shunt through the defect, pulmonary vascular engorgement, a decreased systemic flow, and early decompensation. This does not happen in a case with foramen ovale. Both the stenosis and the atrial septum should be corrected at the same time in order to avoid this sequence of events.

Patent Foramen Ovale with Severe Pulmonary Valvular Stenosis. The foramen ovale, normally patent at birth, remains patent anatomically (but not functionally) in 25 per cent of normal adults. Normally, left atrial pressure, which is higher than the right, keeps the valve functionally closed since the valve of the foramen ovale lies on the left atrial side. However, when right atrial pressure rises above the left, the valve opens and a right-to-left shunt develops. In this malformation, the severe obstruction to the outflow of blood from the right ventricle raises the filling pressure of the right ventricle, thus increasing right atrial pressure and producing a right-to-left shunt through the foramen ovale[8]

Signs and symptoms relate to the pulmonary *stenosis which* causes a decreased pulmonary blood flow, exertional dyspnea, and fatigability. The right-to-left shunt produces *cyanosis.* Heart failure may be present but is not associated, however, with orthopnea or evidence of pulmonary congestion. There is a variable degree of cyanosis and clubbing, a bulge of the left chest, somewhat increased precordial activity, and a forceful right ventricular impulse. The apex of the heart is displaced laterally There is a long, loud, high-pitched *systolic murmur,* associated with a systolic thrill, maximal in the 2d left interspace, equally well heard in the 1st left interspace, and well transmitted upward toward the left clavicle. The pulmonary 2d sound is pure and soft, and diastole is clear. There may be evidence of right heart failure The ECG reveals *systolic overload* of the right ventricle and right ventricular strain On fluoroscopy, the right ventricle and atrium are enlarged The main pulmonary arteries are full and somewhat pulsatile, the distal pulmonary arteries are small and quiet. By angiocardiography, there is a right-to-left shunt at the atrial level, an obstruction to outflow of blood from the right ventricle, and a delayed passage of contrast medium through the lungs The area of valvular stenosis may be visualized. A marked pressure gradient across the pulmonary valve

[6] Theoretically, this increase in the diastolic pressure of the right ventricle should be considered evidence of initial right ventricular failure *Editor*

[7] As the right-to-left shunt bypasses the lungs, these symptoms cannot be attributed to increased pulmonary flow. Rather, they can be explained as the result of left ventricular failure, possibly favored by increased inflow and lower saturation of arterial blood. Editor.

[8] See note 6 *Editor.*

stenosis makes differential diagnosis difficult. The rumble of mitral stenosis, however, is heard maximally at the apex and is well transmitted toward the left axilla, whereas that of functional tricuspid stenosis is heard maximally medial to the apex and transmitted better toward the sternum Cardiac catheterization may establish the diagnosis for, if the left atrium and left ventricle are catheterized, a *diastolic pressure gradient across the mitral valve* will be observed.

THERAPY. This lesion is far less common than it was previously thought The mitral stenosis must be treated at the same time that the defect is closed, or acute pulmonary edema will develop Treatment of an acquired mitral stenosis is relatively simple, but treatment of congenital mitral stenosis may be impossible because of a tiny valve ring and totally malformed leaflets, which are frequently adherent to the endocardium Since the exact abnormality of the mitral ring can be established only during surgery, the patient's prognosis cannot be determined preoperatively.

Septum Secundum Defect with Transposition of the Great Vessels. This rare form of transposition of the great vessels usually causes death in the first few months of life, this is due to severe hypoxia, complicated by congestive failure Pulmonary resistance falls immediately after birth since there is no defect at the ventricular or great vessel level Pulmonary blood flow increases progressively, and pulmonary congestion occurs early Examination of the small arteries of the lungs reveals much less medial hypertrophy than is found in other forms of great vessel transposition Murmurs are usually absent, cardiac failure appears early and is severe. Despite marked cardiomegaly, the left atrium is *not* enlarged Determination of left atrial size, therefore, is essential to the differential diagnosis A left-to-right shunt at the atrial level is demonstrated by catheterization An angiocardiogram in the LAO view shows filling of the left atrium from the right atrium, without evidence of a ventricular defect or patent ductus

THERAPY. This form of transposition of the great vessels is theoretically totally correctable by relocation of the atrial septum in such a manner that venous blood is directed through the mitral valve and oxygenated blood through the tricuspid valve. Such a procedure is facilitated by the absence of other intracardiac defects and the absence of severe pulmonary vascular disease.

Septum Primum Defect with a Cleft Mitral Valve. The position of the septum primum defect differs from the more common form of secundum defect in that the defective area lies just over the tricuspid and mitral valves and involves the septal leaflet of the two valves The separate halves of the mitral and tricuspid septal leaflets fail to fuse completely, thus forming a *cleft leaflet,* which produces mitral or tricuspid insufficiency, or both. In addition to the increased right ventricular work load caused by the septal defect, valvular insufficiency places a burden on the ventricle involved *Mitral insufficiency* is the most common. The volume of blood regurgitated into the atrium from the left ventricle increases pulmonary venous pressure. As a consequence, some degree of pulmonary hypertension is retained after birth and a normal development of the pulmonary vascular pattern is not followed. Thus, a factor of moderate-to-marked pulmonary hypertension complicates the physiologic alterations produced by a simple atrial defect, and frequently produces early right ventricular failure, a right-to-left shunt, and cyanosis

Correct diagnosis is sometimes extremely difficult. The presence of a *large left ventricle* differentiates this malformation from a simple secundum defect, but does not differentiate it from either an atrioventricularis communis or a large ventricular defect A normal-sized left atrium differentiates this malformation from a large ventricular defect, but not from an atrioventricularis communis. The early development of cardiac failure in a child with an atrial defect should make one suspicious of a primum defect associated with a cleft mitral valve. The murmurs usually associated with an atrial defect are heard, and in addition, there is a systolic murmur at the apex which radiates laterally and suggests mitral insufficiency Under the fluoroscope, both ventricles and the right atrium are enlarged. The left atrium is normal The ECG shows evidence of *biventricular enlargement* and *hypertrophy* without evidence of left atrial enlargement. Cardiac catheterization demonstrates the presence of a large left-to-right shunt at the atrial level. Blood samples from the right

gestive of vascular disease rather than pulmonary stenosis

The chief differential diagnostic tool is cardiac catheterization. The absence of a pressure gradient across the pulmonary valve is demonstrated, if the pulmonary artery is catheterized. Pulmonary capillary pressure is normal. Arterial unsaturation is present. On angiocardiography, a right-to-left shunt at the atrial level is present, there is delayed passage of contrast medium through the lungs, and the major pulmonary vessels narrow suddenly as they leave the hilum

THERAPY Successful therapy for this disease awaits clarification of its etiology. The use of *vasodilator drugs* has been advocated and appears to have promise if the disease process is recognized during the stage of marked medial hypertrophy of the small pulmonary vessels and before excessive intimal proliferation has developed Unfortunately, however, this stage frequently occurs before symptoms have developed If vasodilators appear to improve the patient's condition, the advisability of a complete therapeutic bilateral *pulmonary denervation* should be considered

Patent Foramen Ovale with Ebstein's Malformation of the Tricuspid Valve In this condition, the origin and structure of the tricuspid valve are abnormal, the septal leaflet arising well within the body of the right ventricle and not from the AV ring Consequently, a portion of right ventricle is included in the right atrium and becomes thin-walled like the wall of this chamber This produces a *high* incidence of ventricular and atrial arrhythmias The tricuspid leaflets are usually thickened and the chordae tendineae are abnormally arranged Both because of origin and structure, the flow of blood from the right atrium to the outflow tract and to the pulmonary artery is obstructed The more extreme the valvular displacement, the greater the obstruction to the blood flow Inflow or outflow obstruction increases filling pressure of the functioning right ventricle, which in turn increases right atrial pressure and produces a right-to-left shunt through a patent foramen ovale.

The signs and symptoms stem from either conduction disturbance or blood-flow obstruction The repeated occurrence in a patient of *supraventricular tachycardia*, *ventricular tachycardia*, or *atrial flutter* with varying block is suggestive More commonly, however, the symptoms are those of exertional dyspnea and moderate cyanosis, with evidence of right ventricular failure. The heart is enlarged, the apex is displaced laterally, a bulge of the left chest may be present, but the precordium is *surprisingly quiet*. Murmurs are notoriously unpredictable. A short, rather insignificant basal systolic murmur is frequently associated with a mid-diastolic murmur heard low over the sternum or out toward the apex. The pulmonary 2d sound is usually split, but not accentuated Fluoroscopically the right ventricle and right atrium are grossly enlarged, but the amplitude of pulsations is decreased. The main pulmonary artery segment is not enlarged, and the peripheral lung fields appear normally vascular. The ECG is not specific, though the common pattern is that of a small wide RSR' pattern in the right chest leads and a notched, slurred, shallow S wave over the left chest leads Occasionally, however, the pattern is that of left ventricular hypertrophy or left BBB. The P wave is frequently peaked The finding of a normal right ventricular and pulmonary artery pressure, associated with a lowered arterial oxygen saturation, suggests either Ebstein's malformation of the tricuspid valve or pulmonary arteriovenous aneurysm A slow pullback maneuver from the right ventricle into the right atrium may establish the abnormal valvular position In the angiocardiogram, the right atrium appears grossly enlarged and empties slowly, and a right-to-left shunt at the atrial level may be present.

THERAPY There is no known corrective therapy for this malformation. Medical therapy should be directed toward the control of cardiac arrhythmias. The efficacy of digitalis, quinidine, Pronestyl, and atropine should be tested by trial and error.

Secundum Defect with Acquired or Congenital Mitral Stenosis. (Lutembacher's Syndrome). The life history of a septum secundum defect is accentuated and shortened by mitral stenosis which increases the pressure of the left atrium and thus increases the volume of left-to-right shunt, producing symptoms at an earlier date The high frequency of a mid-diastolic rumble caused by relative tricuspid

atrium, the valve may be approached from the right chest, thus eliminating opening the left chest. The operation should be carried out using inflow occlusion and extracorporeal circulation.

GROUP III: DEFECTS OF PULMONARY VENOUS DRAINAGE

Total anomalies of the pulmonary venous return are characterized by the drainage of both right and left pulmonary veins into a *common vein* which passes behind the heart and joins the systemic venous return at the level of (1) the superior vena cava, (2) the left innominate vein, (3) the right atrium, (4) the coronary sinus, or (5) the portal system below the diaphragm. The differential diagnostic points which are helpful in localizing the site of entry of the common pulmonary vein will be reviewed after a general discussion of the hemodynamic alterations.

Total anomalous pulmonary venous return to the right side of the heart must be considered separately from atrial defects of any type because of the difference in hemodynamics existing prior to birth. In the normal fetus, a significant volume of blood passes from the right ventricle through the lungs to the left atrium and ventricle This volume augments blood flow from the right atrium to the left through the patent foramen ovale, so that the total left ventricular output approaches that of the right ventricle. When the pulmonary veins return to the right side of the heart, the volume of blood reaching the left side of the heart is greatly reduced Consequently, the left ventricle and atrium are abnormally small, despite the fact that, after closure of the patent ductus arteriosus, they must accept the total responsibility for systemic flow The volume of systemic blood flow in early infancy may be small but probably increases gradually as a result of right ventricular failure and increased right atrial pressure After birth, the absence of venous return to the left atrium prevents left atrial pressure rise and foramen ovale closure, so that *a right-to-left shunt* through the foramen continues

In contrast to the left ventricle, the fetal right ventricle handles a large volume of blood and consequently is abnormally thick and large. This increased blood volume perfuses the lungs following birth and closure of the ductus. The major portion of blood returning to the right atrium passes again to the lungs because the small foramen ovale and small size of the left ventricle have increased the filling pressure of the left side of the heart A pulmonary flow, many times that of systemic flow, develops within the first few minutes of life. Pulmonary pressure remains high since the volume of pulmonary blood flow is sufficient to utilize the major portion of the increased pulmonary vascular bed Thick-walled pulmonary vessels persist, and pulmonary vascular disease develops early. High pulmonary blood flow and high pulmonary artery pressure result in early right ventricular failure and a hemodynamic alteration which has the beneficial effect of increasing right ventricular filling pressure and shunting a large volume of blood from the right atrium to the left. Unfortunately, right ventricular failure also increases pulmonary venous pressure and leads to a more rapid development of pulmonary vascular disease.

The large pulmonary blood flow which is present immediately after birth produces symptoms in infancy. Dyspnea, mild cyanosis, fatigability, and susceptibility of pulmonary infections are common. Early evidence of right heart failure and pulmonary congestion depend upon the degree of pulmonary vascular disease and the volume of pulmonary blood flow Peripheral pulses are of poor quality during infancy, although they may be normal in the older child There is a bulge of the left chest, and precordial activity is markedly increased A strong apical impulse is felt across the lower precordium, and a forceful pulmonary second thrust is felt at the base. The apex of the heart is displaced laterally. A systolic murmur, suggestive of relative *pulmonic stenosis*, is usually present at the base of the heart. A mid-diastolic rumble near the apex, well transmitted into the left sternal border, suggests *relative tricuspid stenosis*. A long decrescendo diastolic blow indicative of *pulmonic insufficiency* may be heard along the left sternal border. The 2d sound is accentuated and split. In less than 50 per cent of patients there is a *continuous bruit*, soft and low-pitched in quality, over the site of entry of the pulmonary veins into the systemic circulation. Evidence of right heart failure and pulmonary congestion may be present. Under

atrium should be obtained close to the tricuspid valve as well as in the midatrium, for the position of the septal defect leads to the streamlining of blood *from* the left atrium into the right ventricle without atrial mixing, except close to the tricuspid valve. Pressure tracings from the left atrium suggest AV valve insufficiency. Right ventricular and pulmonary artery pressures are elevated frequently to the degree where a diagnosis of a large ventricular defect is suggested. Comparative dye-dilution studies from the left atrium and left ventricle establish whether an additional ventricular defect is present and constitute the only reliable method of determining whether the ventricular septum is intact or not. An angiocardiogram reveals reopacification of the right side of the heart and frequently a small right-to-left shunt at the atrial level.

THERAPY Treatment of this malformation should be carried out in early childhood because of the relatively severe and rapidly progressive pulmonary vascular disease. Blind methods of closure are not applicable here since the valvular insufficiency must be corrected at the same time and must be done under direct vision. The septal defect is closed with an Ivalon sponge, and the cleft in the mitral or tricuspid valve is obliterated by sutures. If there is an associated ventricular defect, the septal leaflet of the tricuspid and mitral valve may be displaced inferiorly to join the ventricular septum, or an additional Ivalon sponge may be used. The latter procedure is indicated if displacement of the mitral septal leaflet is sufficiently marked to create aortic stenosis. If a widely cleft valve is present, a valvular graft may be necessary to prevent postoperative mitral and tricuspid stenosis.

Septum Secundum Defect with Mitral Insufficiency Mitral insufficiency may be produced by shortening of the chordae tendineae and faulty development of the mitral valve, although a cleft is not present and the defect does not extend to the AV ring. Signs and symptoms are similar to those of a septum primum defect and cleft mitral valve. The therapeutic approach is identical.

Small Patent Foramen Ovale with Congenital Mitral Stenosis. The principal alteration in hemodynamics is caused by the mitral stenosis and the increased pulmonary venous pressure. The magnitude of the left-to-right shunt is reduced by the small size of the partially closed foramen ovale. The pattern of pulmonary hypertension is complicated by venous congestion, capillary dilatation, thickening of the alveolar walls, and the presence of *pulmonary edema* because of increased pulmonary venous pressure prior to birth. The left atrium is large when the foramen ovale is of moderate size, but when the foramen ovale is barely patent, the left atrium is abnormally small since fetal right ventricular blood flow is directed almost totally through the ductus because of the increased pulmonary venous resistance.

The changes occurring in the lungs before birth make extremely difficult the shift from reliance on the placenta to reliance on the lungs for gaseous exchanges. The newborn infant appears acutely ill, cyanosis due to right heart failure and faulty gaseous diffusion appears early, pulmonary hypertension is severe. The peripheral pulses are poor, the apex of the heart is displaced laterally. Murmurs may be present, suggesting mitral stenosis possibly combined with insufficiency. There is evidence of right heart failure and pulmonary congestion. Under the fluoroscope, the lungs appear vascular and congested. The right side of the heart is enlarged, the left ventricle is normal, and the left atrium is normal or enlarged. Right ventricular strain is revealed by the ECG. Contrast solution traverses the lungs slowly, and there may be reopacification of the left atrium with each beat of the heart, indicating mitral insufficiency. The obstructed mitral orifice, as well as a small left-to-right shunt across the foramen ovale, may also be seen. Pulmonary artery pressure is markedly increased, and a high pulmonary wedge pressure is found, which indicates severe pulmonary venous obstruction.

THERAPY Correction of this malformation, though extremely hazardous, must be undertaken in early infancy. The outcome is dependent upon the magnitude of pulmonary vascular disease and the exact type of mitral obstruction. Little can be done if the mitral ring is abnormally small and the valve itself is normal. However, if there has been fusion of the leaflets of the mitral valve, it may be possible to open the valve. Because of the size of the patient and the size of the left

alous pulmonary drainage because there is a narrowing of the common pulmonary vein as it passes through the diaphragm, which adds the factor of pulmonary venous obstruction to the total picture Capillary and alveolar changes occur prior to birth, which cause a barrier to gaseous diffusion immediately after birth. Infants with this anomaly appear cyanotic within hours after birth. Cyanosis and dyspnea increase rapidly There may be early evidence of right heart failure Murmurs are usually absent The pulmonary 2d sound at the base of the heart is *accentuated* and *split*, and an *early diastolic murmur* of pulmonary insufficiency may be present along the left sternal border. The lungs are usually clear. In addition to the enlargement of the right side of the heart and the main pulmonary artery segment as seen by x-ray, the lungs have a finely granular appearance similar to that caused by severe congestion in acquired mitral stenosis There is laboratory evidence of a right-to-left shunt at the atrial level, and occasionally of reopacification of the inferior vena cava after passage of the contrast medium through the lungs.

THERAPY. Therapy for this malformation must be undertaken in the first weeks of life because life expectancy is short and the development of pulmonary vascular disease is rapid. Unfortunately, the diagnosis is usually made at the autopsy table If diagnosed early, however, correction of the defect with closure of the patent foramen ovale should be possible

GROUP IV: MALFORMATIONS WITHOUT A COMMUNICATION BETWEEN THE SYSTEMIC AND PULMONARY CIRCULATIONS

Lesions of the Left Side of the Heart without Elevated Pulmonary Venous Pressure at Birth

Coarctation of the Aorta. This malformation is characterized by an extreme narrowing of the lumen of the aorta immediately distal to the origin of the left subclavian artery at the point of the insertion of the ductus arteriosus. The obstruction to aortic blood flow places a strain upon the left ventricle, and the arterial blood pressure proximal to the coarctation is elevated. Vascular pathways connecting the proximal and distal aortic segments form a large network of *collateral arterial vessels* and increase the blood flow to the lower extremities. Circulatory embarrassment is rare during infancy. In a few patients, when the entire load of maintaining the systemic circulation against a high resistance is placed on the left ventricle, congestive failure may appear after closure of the ductus Death may result, or the patient may develop sufficient left ventricular hypertrophy to reestablish cardiac compensation. In most patients, symptoms are absent during childhood, and the malformation is suspected for the first time when *arterial hypertension* is discovered during a routine physical examination There is a surprising sex distribution which confines this malformation to *males* by a very large percentage. Because blood flow is increased to the upper extremities and decreased to the lower extremities, the patient with a coarctation of the aorta has broad shoulders, a well-developed chest, and relatively narrow hips.

Early symptoms are *pains and cramps in the legs,* numbness, cold lower extremities, and frequently severe *headaches* The advanced symtoms are those of severe hypertension or congestive failure

The pathognomonic physical finding of coarctation of the aorta is the *absence* or *weakening of the femoral artery pulse* and a decrease in femoral artery systolic pressure. In contrast to the sharp forceful radial pulse, the femoral pulse feels dampened, has a narrow pulse pressure and a late peak because of prolonged ascending and descending limbs of the pulse wave Pulsations of the abdominal aorta are also weak or absent A *systolic murmur,* loudest during midsystole, is heard at the base of the heart and along the spine posteriorly The midsystolic timing suggests that the murmur arises outside the heart. In older individuals, *continuous or systolic bruits,* which suggest a markedly increased collateral blood flow, may be heard over the intercostal vessels, along the course of the internal mammary vessels, or in the axilla The *aortic 2d sound is increased in intensity* Not infrequently, there is a *decrescendo diastolic murmur,* maximal over the aortic valve area and heard along both sides of the sternum, which suggests aortic insufficiency and an associated congenital bicuspid aortic valve. Enlarged intercostal vessels may be palpated over the chest.

the fluoroscope, the right side of the heart and the pulmonary artery are enlarged, and the pulmonary vascular markings are increased. The aorta may be small. The ECG reveals *right axis deviation* and a *right BBB* pattern suggestive of combined diastolic and systolic overload of the right ventricle. The presence of a uniform oxygen content in blood samples from the right atrium through the right side of the heart and including systemic arteries is pathognomonic. Pulmonary artery pressure is elevated, systemic pressure is low In the angiocardiogram there may be a filling *defect* at the site of entry of the anomalous pulmonary veins, and both right and left sides of the heart opacify simultaneously Reopacification of the right side of the heart occurs after circulation of the contrast medium through the pulmonary vascular bed

THERAPY Total correction of this malformation includes closure of the foramen ovale and the creation of a sufficiently large anastomosis between the common pulmonary vein and left atrium to prevent obstruction of the pulmonary venous return It is difficult to make a sufficiently large anastomosis unless the right atrium is opened. The atrial septum is incised, and the common pulmonary vein, which lies immediately posteriorly to the left atrium, is anastomosed to the left atrium from within the left atrial cavity, utilizing a long incision parallel to the course of the common pulmonary vein In part, the success of the correction is dependent upon the ability of the underdeveloped left side of the heart to handle an increased systemic blood flow Unfortunately, accurate estimation of systemic blood flow prior to surgery is extremely difficult since a true mixed venous sample from the systemic circulation cannot be obtained Correction of the defect should be carried out before excessive pulmonary vascular disease has developed Inflow occlusion and an extracorporeal circulation are necessary adjuncts to the surgical procedure Care must be taken to drain bronchial artery blood flow from the lungs during the period that the common pulmonary vein is closed and thus prevent pulmonary hemorrhage Left heart failure may be avoided by closing the atrial defect with an Ivalon sponge which contains several 4-mm holes in order to permit decompression of the left atrium Experimental evidence suggests that these holes will endothelialize within few days and thus complete the closure.

Total Anomalous Pulmonary Venous Return to the Superior Vena Cava. In this malformation, the common pulmonary vein usually enters the superior vena cava close to the entry of the azygos vein. A *continuous murmur* may be heard to the right of the midline in the 2d and 3d interspace Under the fluoroscope, there is a prominent bulge of the superior vena cava Cardiac catheterization reveals a sudden increase in oxygen *content in* the superior vena cava above the insertion of the cava into the right atrium. With angiocardiography, there is reopacification of the superior vena cava after the contrast medium has passed through the *lungs*

Total Anomalous Pulmonary Venous Return to the Left Innominate Vein. This malformation may be differentiated radiographically from the insertion of the common pulmonary vein into the superior vena cava by means of a bulge, which gives the heart a figure-of-eight appearance that is seen above the level of the main pulmonary artery segment both to the left and right of the midline. There is an increased oxygen content of blood sampled from the bulge, and this area reopacifies in the angiocardiogram.

Total Anomalous Pulmonary Venous Return to the Right Atrium. The differentiation of this malformation from a large atrial septal defect is difficult The correct diagnosis depends upon the demonstration of *a common oxygen content in the right atrium, right ventricle, pulmonary artery, and aorta,* bidirectional shunt at the atrial level, and simultaneous filling of the pulmonary artery and aort

Total A [illegible]

[illegible] pulmonary vein enters the coronary sinus, causing a localized bulge of the right atrial contour. There is reopacification of the coronary sinus following the passage of contrast solution through the lungs An increase in oxygen content of the blood of the coronary sinus is demonstrated by cardiac catheterization.

Total Anomalous Pulmonary Venous Drainage into the Portal System. The clinical syndrome associated with this malformation is totally different from other varieties of anom-

symptoms of early left heart failure. Surgery should not be delayed unduly for congenital aortic stenosis causes sudden death in about 10 per cent of patients.

Subaortic Stenosis. In this malformation, the aortic valve is normal. Immediately proximal to the aortic valve, a fibrous band partially occludes the outflow tract of the left ventricle. Subaortic stenosis simulates valvular aortic stenosis for the signs and symptoms are identical, and differential diagnosis is difficult. A clearly *split 2d sound* at the base of the heart suggests subaortic rather than aortic stenosis. Poststenotic dilatation of the ascending aorta occurs in both. However, in valvular stenosis, the dilatation is distal to the sinuses of Valsalva and a clear incisura is seen on x-ray which separates the right atrium from the ascending aorta. In subaortic stenosis, the dilatation extends right to the valve ring, thus obscuring the incisura. Left heart catheterization may establish the diagnosis if, on pullback into the left ventricle, one can demonstrate an area of systolic pressure equal to that of the aorta and a diastolic pressure of zero.

THERAPY. The therapeutic approach to this malformation is the excision of the subaortic band through the ascending aorta under direct vision, using *inflow occlusion and extracorporeal circulation*.

Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery. This is a rare deformity in which the left coronary artery arises from the pulmonary artery. Blood to the left myocardium has a lower oxygen content, and when pulmonary artery pressure is normal, the perfusion pressure is too low to be effective. During left ventricular contraction, the pressure applied to the outer wall of the intramyocardial coronary arteries exceeds intravascular pressure and blood may be forced back into the pulmonary artery. The rate of perfusion is thus greatly reduced, and myocardial ischemia and infarction may result. Signs and symptoms are absent at birth because pulmonary artery pressure is high. It is only when pulmonary artery pressure drops and the difference between systemic and pulmonary pressure becomes significant that myocardial ischemia develops. Symptoms usually occur between the second and sixth month, and death follows relatively rapidly. The symptoms are of two types. Attacks may be brought on by a meal and are characterized by intense precordial pain accompanied by pallor, cyanosis, cold perspiration, and rapid respirations. On the other hand, initial symptoms may involve only the respiratory apparatus, leading to the frequent diagnoses of pneumonia. Combined heart failure may be present. The heart is large and quiet; heart tones are poor and distant, and murmurs are seldom heard. The apical heart beat is difficult to feel, and *heart sounds over the right ventricle are louder than those over the left.* Under the fluoroscope, the left ventricle and left atrium appear huge. Pulsations of the left ventricle may be difficult to see. The electrocardiographic pattern may be one of *left heart strain* or may suggest a myocardial infarct. Characteristically, the T waves are deeply inverted in the standard limb and left precordial leads, and the amplitude of the QRS complex is reduced. Occasionally, a deep Q wave may be present in leads I and aVL and a QS pattern may be seen in the left chest leads. The origin of the left coronary from the pulmonary artery has been demonstrated by angiocardiography. The left ventricle appears large and thin-walled in contrast to the small-chambered, thick-walled left ventricle of endocardial fibroelastosis.

THERAPY. The surgical correction of this anomaly may be possible provided that the diagnosis can be made early enough and adequate perfusion of the left coronary vessel can be maintained during the anastomosis of the left coronary vessel to a systemic artery. Ligation of the left coronary or the use of talc in the pericardium has been of some success, but the long-term prognosis would not appear so good as if an adequate flow through the anomalous coronary could be brought about by an anastomosis.

Endocardial Fibroelastosis. It has not been definitely established whether or not this condition represents a congenital malformation.[11]

The etiology may well be metabolic rather than a specific congenital malformation. There is a marked thickening of the endocardium, of the left ventricle, of the left atrium, and occasionally of the right side of the heart. Elastic fibers are abundant and infiltrate adjacent myocardium. The myocardium is greatly hypertrophied. The thickened endocardium and hypertrophied myocardium suggest that the mechanism is similar to that of con-

[11] See Part 18, Chaps. 12 and 13. *Editor.*

Fluoroscopic examination reveals an enlargement of the left ventricle, anterior rotation of the apex, and a boot-shaped heart. The main pulmonary artery segment is not well visualized in the PA position. A careful study of the base of the heart, with the patient in a slight LAO view and with the esophagus filled with barium, frequently reveals the area of coarctation and poststenotic dilatation. In children over the age of 10, *scalloping of the lower ribs* may be seen on x-ray, which indicates erosion of the inferior margin of the rib by the enlarged and tortuous intercostal vessels The ECG may be normal or may give evidence of left ventricular hypertrophy. Angiocardiography and cardiac catheterization are seldom necessary to establish the diagnosis. When the length of the narrow aortic segment is in question, a *retrograde aortogram* offers the best means of defining the obstruction.

THERAPY The long-term success of surgical resection of aortic coarctations warrants operation for the child, even though the patient may be completely asymptomatic. Prolonged hypertension causes progressive arteriosclerotic changes proximal to the coarctation, so that surgery should be advised *during childhood*. The optimal time for correction is 8 to 15 years of age, but in the presence of severe congestive failure, surgery may be carried out at any age The use of *a graft* may be necessary if the coarcted segment is long

A special therapeutic problem concerns the infant with a simple coarctation and severe congestive failure All measures for the medical treatment of congestive failure should be attempted first and a period of watchful waiting advised If failure reappears, early surgery is mandatory.

Aortic Stenosis. Congenital valvular aortic stenosis occurs more frequently than previously thought During childhood, the valve is thickened, rubbery, and fibrous, with leaflets which are partially or totally fused. During adulthood, calcification occurs and the anatomic differential diagnosis between rheumatic and congenital aortic stenosis becomes difficult, if not impossible Stress placed on the left ventricle increases with the passage of time because progressive changes in the valve increase the degree of stenosis, and there is a steady increase in cardiac output as the patient grows and develops. A stenosis, which is of little significance while cardiac output is low, becomes highly significant if cardiac output is doubled or tripled. This accounts for the common appearance of symptoms near the age of puberty.

Symptoms are absent until failure of the left ventricle occurs The common symptoms are fatigability, exertional dyspnea, and occasionally *syncope* or precordial pain. The peripheral pulses are full and equal, and the pulse pressure is normal in the asymptomatic patient; in the patient with symptoms, however, the pulse wave is slow and the pulse pressure is narrow. A forceful apical impulse felt to the left and below the site of the normal apical beat is present. A *systolic thrill* is palpable at the base and frequently extends into the neck. A loud, long, frequently high-pitched *systolic murmur* is heard in older patients in the 1st and 2d right interspace and is well transmitted to the neck During infancy, the murmur is maximal in the 3d and 4th left interspace, suggesting the diagnosis of ventricular defect. As the child grows, the murmur becomes louder at the base, first to the left and then to the right of the sternum A long systolic murmur extending throughout systole suggests greater obstruction than a short and coarse systolic murmur. The 2d sound at the base of the heart is clear. Under the fluoroscope, the apex of the heart is rounded and anteriorly rotated so that, in the PA projection, the pulmonary artery area is concave and the ascending aorta is prominent. If there is left heart failure, the left atrium may be enlarged. The ECG reveals left ventricular hypertrophy. Left heart catheterization, when the catheter is passed through the aortic valve, confirms the presence of a *pressure gradient across the aortic valve*

THERAPY. Surgical correction is best accomplished using inflow occlusion and direct vision of the valve through the open ascending aorta with either *hypothermia* or an *extracorporeal circulation*.[10] Great care must be taken to incise the valve down to the valve ring along the line of the commissure in order to avoid significant postoperative aortic insufficiency. Indications for surgery are the progressive development of left ventricular hypertrophy or strain in the ECG and the appearance of

[10] See also Part 7, Chap 16. *Editor*

trophy. The striking finding in an angiocardiogram is the *slow passage of contrast medium through the lungs* and the retention of a large volume of radiopaque material in the greatly enlarged left atrium. Repeated reopacification of the left atrium suggests significant mitral insufficiency. Cardiac catheterization is of little value. Pulmonary wedge pressure is elevated.

THERAPY. The successful surgical correction of this malformation depends upon the type of mitral stenosis which is present Little can be done for the patient if the mitral valve ring is markedly reduced in size However, if the stenosis is primarily due to fusion of the commissures, a mitral commissurotomy may be helpful Inflow occlusion and extracorporeal circulation should be used, so that the malformed valve can be visualized readily. Early surgery should be advised because of the rapidly progressive pulmonary vascular disease.

Cor Triauriculare

In this malformation, the embryonic common pulmonary vein fails to be absorbed into the wall of the left atrium, and the junction of this common vein with the atrium is stenotic. Increased pressure in the common vein invaginates it into the left atrium, producing a formation like an appendage within the atrium The stenotic orifice of the vein takes a position close to the mitral valve and produces the clinical picture of mitral stenosis

A *foramen ovale* is usually present and opens into the lower or true left atrial chamber Occasionally, the upper chamber and right atrium may be connected by an anomalous pulmonary vein or window opening More rarely, the upper chamber is blind, except for an opening into the right atrium, and blood from the pulmonary veins reaches the left ventricle after traversing the upper left atrial chamber, thence through the atrial defect into right atrium, and then via the foramen ovale into the lower left atrial chamber, and finally through the mitral valve into the left ventricle.

The clinical findings are those of mitral stenosis associated with either advanced *pulmonary vascular disease* or episodes of *acute pulmonary edema,* depending upon the severity of the stenosis. A bulge of the left chest is present. There is an *apical mid-diastolic rumble* with presystolic accentuation Systole is clear. A *decrescendo diastolic murmur* of pulmonary insufficiency may be heard along the left sternal border. There is enlargement of the right side of the heart and the left atrium under the fluoroscope. In contrast to congenital and acquired mitral stenosis, the left auricular appendage is not enlarged since the inner wall of the left atrium formed by the common pulmonary vein does not include the latter. The ECG shows a right ventricular hypertrophy Pulmonary arterial and pulmonary wedge pressures are elevated. A significant *pressure gradient* between pulmonary arterioles (pulmonary wedge pressure) and left atrium indicates some form of *pulmonary venous obstruction*

THERAPY. Prognosis with surgery should be excellent, for the release of the stenotic common pulmonary vein outlet reestablishes a normal circulation without injury to the mitral valve Surgery should be advised as early as possible for the optimal prognosis is limited by the progressive development of pulmonary vascular disease.

Congenital Pulmonary Venous Obstruction. This malformation may be a primary congenital defect or the result of endocardial fibroelastosis It may involve all or only one of the pulmonary veins. Damage to the parenchyma of the lung from elevated venous pressure may occur before birth, shortly after birth, or later, depending upon the severity and the number of veins involved. The symptoms are those of *cor pulmonale* progressive exertional dyspnea, fatigability, episodes of hemoptysis, and right heart failure There is a bulge of the left chest and increased amplitude of right ventricular contractions. Murmurs are usually absent, however, a *systolic murmur* of relative pulmonary stenosis and a *diastolic murmur* of pulmonary insufficiency may be heard along the left sternal border The *2d heart sound is loud and split* Under the fluoroscope, only the right side of the heart is enlarged. The lung fields usually appear clear, but there is enlargement of the main pulmonary arteries The ECG reveals *systolic overload of the right ventricle,* and the *tall P waves* of right atrial hypertrophy may be present The angiocardiogram demonstrates the slow passage of contrast medium through the lungs and a normal-sized left atrium Pulmonary artery and pulmonary wedge pressures are markedly elevated.

THERAPY The therapeutic approach to this malformation is based on early diagnosis and early surgical relief of the pulmonary venous stenosis. The success is entirely dependent upon the time at which the diagnosis is made,

strictive pericarditis in that the left ventricle cannot reduce its chamber size during contraction and expel blood during systole because of the dense endocardium End diastolic pressure is high, and systolic pressure is low

The onset of symptoms occurs most frequently during the first six months of life and, in 95 per cent of cases, during the first year. The most common presenting complaint is *pneumonia* Signs of left and right heart failure are present The heart is grossly enlarged, but the precordium is quiet. Heart tones are normal or reduced *Murmurs* arising from the mitral valve, and occasionally from the aortic valve, are frequently present and help to differentiate this lesion from anomalous origin of the left coronary artery An apical systolic murmur is most common A triple (gallop) rhythm may be present Under the fluoroscope, the heart appears grossly enlarged, with primary enlargement of the left ventricle and left atrium Cardiac activity is decreased, and the lungs frequently appear congested The ECG shows severe left heart strain and marked left ventricular hypertrophy A delayed passage of contrast medium through the lungs, an enlarged left atrium, and large, very thick-walled left ventricle are seen in the angiocardiogram Pulmonary arterial and pulmonary wedge pressures are of little value. The chief differential diagnostic findings to distinguish this malformation from anomalous origin of the left coronary artery are marked left ventricular hypertrophy and strain in the ECG, and a thick-walled, small-chambered left ventricle visualized by angiocardiography

THERAPY The efficacy of treatment cannot be judged since it is extremely difficult to prove the diagnosis without an autopsy Medical treatment consists of antibiotics, digitalis, mercurial diuretics, low salt diet, and oxygen The response to digitalis is sometimes dramatic It now seems clear that there is a real chance for recovery if the infant survives the first attack of failure and responds well to digitalis Repeated attacks of pneumonia and left heart failure occur in infancy, but over a period of years the attacks decrease and may eventually disappear Whether this improvement results from a decrease in thickness of the endocardium or increased efficiency of the left ventricle is not clear

The surgical approach, which theoretically offers the best chance of physiologic correction, is an *endocardectomy* which, just as a pericardectomy for constrictive pericarditis, restores normal function. However, the question of mural thrombus formation, embolization, and recurrence of endocardial scarring remains to be answered.

LEFT-SIDED LESIONS ALWAYS ASSOCIATED WITH AN ELEVATED PULMONARY VENOUS PRESSURE

Congenital Mitral Stenosis. Isolated congenital mitral stenosis is rare, for some degree of mitral insufficiency is almost always present. The malformed mitral valve has abnormally shortened chordae tendineae, fused commissures, thickened valve leaflets, and frequently, an abnormally small valve ring.

When stenosis is severe, increased pulmonary venous pressure is present prior to birth, and fetal pulmonary hypertension is retained and complicated by *alveolar and capillary wall thickening*, with resultant diffusion difficulty. Extreme dyspnea, fatigability, cyanosis, and the early onset of right-sided congestive failure without evidence of pulmonary congestion characterize this syndrome. When stenosis is less severe, vascular and parenchymal changes do not occur prior to birth, for the mitral valve can accommodate the small fetal pulmonary blood flow. After birth, the rapidly increasing pulmonary blood flow makes the mitral stenosis progressively more significant. Pulmonary venous hypertension develops, and in addition to the findings of right heart failure, the clinical pattern is characterized by episodes of severe *pulmonary edema*

In most patients, an *apical systolic murmur* indicative of some degree of mitral insufficiency is present, in addition to the *diastolic rumble* of mitral stenosis The 2d heart sound at the base is *accentuated* and *split*, and a *decrescendo diastolic* murmur of pulmonary insufficiency is frequently heard along the left sternal border. Under the fluoroscope, the heart presents an enlargement involving primarily the left atrium and right ventricle. Left ventricular enlargement is also present if mitral insufficiency is significant The lung fields appear congested. The pulmonary arteries are enlarged The electrocardiographic pattern is that of *right ventricular hypertrophy* and a wide notched P wave suggestive of *left atrial hyp-*

of the major pulmonary arteries, which may be congenital in origin or represent healed thrombi. The most striking physical finding is a *loud, long systolic murmur, heard over the entire pulmonary bed* and which, in certain areas, may be *continuous*. The pulmonary 2d sound at the base of the heart may be either accentuated or normal. Evidence of right ventricular hypertrophy and right heart failure may be present if the total sum of stenotic areas is great.

The diagnosis of this malformation is best confirmed by angiocardiography, for with filling of the pulmonary arterial trunk, the multiple areas of stenosis stand out. Pressure gradients may be found within the larger pulmonary vessels indicative of some degree of peripheral stenosis.

THERAPY. In patients in whom the stenosis is membranous and immediately distal to the pulmonary valve, excision of the stenotic area may be curative. When the areas of stenosis are multiple, the best that can be achieved is the relief of the most extreme sections.

strictive pericarditis in that the left ventricle cannot reduce its chamber size during contraction and expel blood during systole because of the dense endocardium. End diastolic pressure is high, and systolic pressure is low.

The onset of symptoms occurs most frequently during the first six months of life and, in 95 per cent of cases, during the first year. The most common presenting complaint is *pneumonia*. Signs of left and right heart failure are present The heart is grossly enlarged, but the precordium is quiet. Heart tones are normal or reduced. Murmurs arising from the mitral valve, and occasionally from the aortic valve, are frequently present and help to differentiate this lesion from anomalous origin of the left coronary artery. An apical systolic murmur is most common A triple (gallop) rhythm may be present Under the fluoroscope, the heart appears grossly enlarged, with primary enlargement of the left ventricle and left atrium Cardiac activity is decreased, and the lungs frequently appear congested The ECG shows severe left heart strain and marked left ventricular hypertrophy. A delayed passage of contrast medium through the lungs, an enlarged left atrium, and large, very thick-walled left ventricle are seen in the angiocardiogram. Pulmonary arterial and pulmonary wedge pressures are of little value The chief differential diagnostic findings to distinguish this malformation from anomalous origin of the left coronary artery are marked left ventricular hypertrophy and strain in the ECG, and a thick-walled, small-chambered left ventricle visualized by angiocardiography.

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setting up the above-described irritative phenomena in the capillaries of the skin.

The time that elapses between the injection and the detection of the ether smell in the nose represents the arm-to-lung time which, in normal individuals and in those suffering from heart failure, is only a fraction of the arm-to-tongue time as measured by the saccharin, Decholin, or calcium methods The interval between the injection of ether and the first appearance on the face of these unpleasant stinging and tingling sensations (which may last only a few seconds) is known as the *arm-to-facial-paresthesia time.* Although the paresthesias are usually confined to the face, they may appear in the scalp or may become generalized, especially in children, where they can extend centrifugally to distant portions of the body. In children, more so than in adults suffering from congenital heart disease, the severity of this cutaneous reaction is proportional to the quantity of ether injected, the most dramatic reaction being obtained when a fuller dose of 5 to 10 minims of ether is employed. The facial paresthesias usually appear at a time coincident with the detection of ether by smell, giving an arm-to-facial-paresthesia time which is equal to the arm-to-lung time The arm-to-facial-paresthesia time may also precede or follow in point of time the arm-to-lung time The arm-to-lung time may, however, register simultaneously with the abbreviated arm-to-tongue time, or it may actually follow the latter If so, this would cause an alteration of the normal relationship between the arm-to-lung time and the arm-to-tongue time. Its fractional arithmetic relationship may thus become altered in right-to-left shunt from a ratio of 1:2 or 1:3, in "normals," to a ratio of 1:1 or 1+:1, in right-to-left shunts.

Positive *paresthesia times* have been obtained in patent ductus arteriosus with complete reversal of the shunt. In three cases of patent ductus arteriosus with a reversed shunt observed by the author, the paresthesias were striking in the lower half of the body of one case, especially in the toes. This is plausible since, as Burchell (1946) has pointed out, more unsaturated (right ventricular) blood reaches the lower than the upper half of the body in this congenital condition. Apparently not enough test substance reaches the conventional signal area to give the classic response In two other similar cases, the facial paresthesias did dominate exclusively, there was undoubtedly sufficient short-circuiting of gaseous ether through a coexisting atrial defect or ventricular defect to trigger off the signal area.

Use of Circulation Times for Localization of Septal Defects during Cardiac Catheterization. The presence of abbreviated circulation time with saccharin or Decholin in congenital heart disease gives only *presumptive* evidence of the presence of a right-to-left shunt. However, the mere qualitative appearance of paresthesias in the course of performing the ether test offers *conclusive* evidence that a right-to-left shunt exists. Obviously the time measurement before paresthesias appear plays no role in such diagnostic conclusion. Valuable as the above conventional methods are, the use of tracer substances injected into a peripheral vein offers inadequate means for the localization of an intracardiac right-to-left shunt However, when these methods are carried out through catheterization, septal defects can be readily localized. Through such means it has become possible to differentiate between the tetralogy of Fallot (with an overriding aorta) and pulmonary valvular stenosis with intact ventricular septum and a patent foramen ovale or an atrial septal defect.

Cardiac catheterization has, therefore, opened new avenues for the differential diagnosis of shunts in congenital heart disease.

The right ventricle-to-systemic-arterial-capillaries time can be determined by the following methods:

Objective Method for Diagnosis of Right-to-left Shunt. FLUORESCEIN METHOD (RIGHT VENTRICLE-TO-FACE TIME) Ziegler has employed fluorescein and ultraviolet light to establish the right ventricle-to-face time. With the catheter in the outflow tract of the right ventricle, a 5 per cent fluorescein with a 5 per cent sodium bicarbonate solution is injected slowly in an amount previously calculated just to fill the entire catheter. An additional amount measured roughly in proportion to body weight is then injected as rapidly as possible The time that elapses from the beginning of the injection to the appearance of the fluorescence in the ocu-

for if advanced pulmonary vascular disease has occurred, little can be gained.

Corrected Transposition of the Great Vessels with Insufficiency of the Left-sided Atrioventricular Valve. Insufficiency of the left-sided tricuspid (functional mitral) valve may be of *two types*. Most commonly, Ebstein's malformation of the valve is present, characterized by the anomalous origin of the septal leaflet from the wall of the systemic ventricle rather than from the AV ring and by malformed shortened chordae tendineae. In contrast to the right ventricle of the classic Ebstein's malformation, the left or systemic ventricle is not abnormally thin, except in the area of ventricle included in the left atrium. Less commonly, the left-sided AV valve is insufficient because of marked shortening of the chordae tendineae, thickening and rolling of the valve leaflets, and anomalous adhesions to the wall of the ventricle. When insufficiency is severe, pulmonary changes occur before birth and persist after birth, *the course is acute*, cyanosis is present if the foramen remains patent, and failure of the right ventricle occurs early. When insufficiency is less severe, the course is characterized by episodes of *acute pulmonary edema* and the gradual production of severe pulmonary vascular disease followed by right ventricular failure and death. The physical findings suggest mitral insufficiency. There is frequently a bulge of the left chest. The apical impulse is displaced laterally and inferiorly, indicating left ventricular enlargement. An *apical systolic murmur* suggests mitral insufficiency. On fluoroscopy, there is marked enlargement of the left atrium and ventricle. Systolic pulsations of the left atrium are easily seen. The lung fields may appear congested. The ECG reveals frequently a *partial or complete AV block*, in addition to the findings of left [illegible]

Th[illegible]

there [illegible]

ciency in early childhood. Proof of the malformation depends upon the establishment of the transposed origin of the aorta and pulmonary artery by angiocardiography or cardiac catheterization. The aorta arises anteriorly and somewhat to the left of the pulmonary artery and frequently produces a straight contour to the left heart border. The pulmonary artery arises in the midline. During cardiac catheterization, the course of the catheter follows a more median position and reaches the pulmonary artery well to the right of the left heart border. Pulmonary artery and pulmonary wedge pressures are usually elevated. Evidence of a shunt is lacking, unless the valvular deformity is associated with a septal defect.

THERAPY. There is no known therapy for this malformation. In the presence of severe pulmonary congestion, the Cutler procedure might be of practical value. *An anastomosis between the azygos vein and a pulmonary vein* might serve to decompress the pulmonary venous engorgement by transmitting stress to the systemic venous system and thus relieve the frightening symptoms of pulmonary edema and protect the embarrassed respiratory function.[12]

RIGHT-SIDED LESIONS

Valvular Pulmonary Stenosis with Intact Ventricular Septum and Closed Foramen Ovale. This malformation differs from isolated pulmonary stenosis with patent foramen ovale in that there is no right-to-left shunt. Cyanosis is absent, except as a manifestation of congestive heart failure. The clinical syndrome is described under isolated valvular pulmonary stenosis associated with a patent foramen ovale.

Isolated Infundibular Pulmonary Stenosis with Intact Ventricular Septum and Closed Foramen Ovale. Except for the absence of cyanosis, this condition does not differ from isolated infundibular pulmonary stenosis associated with patent foramen ovale.

Primary Pulmonary Hypertension with Closed Foramen Ovale. This entity is similar to pulmonary hypertension associated with patent foramen ovale, except for the absence of a right-to-left shunt through the foramen ovale.

Coarctation of the Pulmonary Arteries. Coarctation of the pulmonary arteries may be divided into two types, the first consisting of a *membranous stenosis* just distal to the pulmonary valve. In this instance, the findings are similar to those of isolated valvular pulmonary stenosis, except for the remarkable distribution of the basal systolic murmur throughout both lung fields. The second type consists of extensive and multiple constrictions

[12] See Chap. 14 Editor.

The curves obtained varied with the site of the defect In the absence of any left-to-right shunt, rapid injection of an indicator into the left atrium, left ventricle, or thoracic aorta yielded a primary curve with a sharp rapid ascent and a slightly slower descent. An injection proximal to the ventricular defect shunted off some of the dye through the pulmonary circulation and caused an abrupt decline in rate of fall in concentration. An injection distal to the site of shunt gave a normal curve This selective injection of indicator into various sites would lead to dilution curves characteristic of the location of the defect and thereby to more precise localization of the left-to-right shunt.

4

Circulation time in congenital heart disease

WILLIAM M. HITZIG

Circulation-time studies not only have served well as screening tests but have contributed considerably to greater understanding of the circulatory dynamics in congenital heart disease Initially employed only for the gross determination of the presence or absence of venoarterial shunt, they subsequently helped to substantiate the findings of angiocardiography and catheterization They have supplied information helpful in differentiating cases with intact septa from others where they were perforated For example, in cases where cyanosis and clubbing may be prominent features, such as pulmonary carcinoma or pulmonary hypertension without shunt, circulation times have been useful in distinguishing these conditions from syndromes with a right-to-left shunt The latter include:

1 Tetralogy of Fallot or Eisenmenger's complex with an overriding aorta

2 Pulmonary valvular stenosis with an interatrial septal defect

3 Interatrial septal defect with pulmonary hypertension and sclerosis

4 Patent ductus arteriosus with reversal of flow

McGuire and Goldman were the first to show that, in certain types of congenital heart disease, the arm-to-carotid-sinus time was considerably abbreviated They regarded this as characteristic of venoarterial shunt, since the substance employed presumably passed from the right heart into the systemic circulation by way of the shunt without traversing the pulmonary circuit

Benenson and Hitzig, who employed saccharin, obtained similar abbreviations of the arm-to-tongue time They realized, however, that a decreased circulation time, although suggestive of right-to-left shunt, is not necessarily diagnostic. Marked anemia or severe thyrotoxicosis may cause a similar abbreviation of the circulation time.

Circulation time was also studied by means of ether (Benenson and Hitzig); this volatile substance sets off cutaneous paresthesias in the systemic circuit which are pathognomonic for a right-to-left shunt.

When 3 to 5 minims of ether is diluted with 10 minims of normal saline and injected, as in tests for determining circulation time, the ether produces unpleasant paresthesias of the skin of the face and subsequently of the extremities, because of the entrance of this substance into the systemic arterial circulation Ordinarily, when ether is injected, it volatilizes and escapes almost completely from the lung during the first circuit of the blood. Only a negligible amount may remain and eventually reach the systemic arterial capillaries, and if so, it never causes any paresthetic phenomena. However, in the presence of a venoarterial communication, ether in variable amounts is shunted into the left side of the heart from where this gas (ether boils at body temperature) is propelled into the systemic circuit,

The curves obtained varied with the site of the defect. In the absence of any left-to-right shunt, rapid injection of an indicator into the left atrium, left ventricle, or thoracic aorta yielded a primary curve with a sharp rapid ascent and a slightly slower descent. An injection proximal to the ventricular defect shunted off some of the dye through the pulmonary circulation and caused an abrupt decline in rate of fall in concentration. An injection distal to the site of shunt gave a normal curve. This selective injection of indicator into various sites would lead to dilution curves characteristic of the location of the defect and thereby to more precise localization of the left-to-right shunt.

lar or oral mucosa represents the right ventricle-to-face circulation time

With this method, a right ventricle-to-face circulation time of 4 sec or less is the average limit between the presence or absence of an interventricular right-to-left shunt. Readings above 4 sec tend to indicate that the shunt is at the atrial rather than at the ventricular level The presence or absence of a ventricular right-to-left shunt may, therefore, be determined by the right ventricle-to-face circulation time, there being an early end point in the latter. In the absence of a ventricular shunt, the degree of prolongation of the right ventricle-to-face time may serve as a possible index to the degree of severity of the pulmonary stenosis

EVANS BLUE (T 1824) (RIGHT VENTRICLE-TO-EAR TIME). Lasser et al employed Evans blue in the determination of the circulation time from the right ventricle to the ear. When the earpiece of a Millikan oximeter was attached to the patient's ear, 5 ml (3 ml in children) of 0 5 per cent aqueous solution of Evans blue (T 1824) was rapidly injected through the cardiac catheter situated in the right ventricle below the tricuspid orifice. The time elapsing between the beginning of the injection (catheter time 0 75 to 1 sec) and the initial deflection of the oximeter galvanometer represented the circulation time from the right ventricle to the ear As the arterial concentration necessary to cause the initial deflection is not known, the values obtained do not really represent the true minimum circulation time, but only the apparent minimum dye appearance time, which varies with the sensitivity and speed of response of the oximeter, and are consequently not comparable with other techniques The average circulation time in cases with a ventricular septal defect was 4 sec (with a range of 3 5 to 4 7 sec) The average of the second group was 7 4 sec (with a range of 5 3 to 10 sec) It was concluded that a *circulation time from the right ventricle to the ear of less than 5 sec is strong evidence of the presence of a right-to-left shunt* through an overriding aorta By this means, such a shunt could be differentiated from that of an atrial septal defect plus pulmonic stenosis Indigo carmine may be substituted for Evans blue in the performance of this diagnostic test for the localization of interventricular shunt.

Subjective Method for Diagnosis of Right-to-left Shunt. ETHER METHOD FACIAL PARESTHESIAS OR (RIGHT VENTRICLE-TO-FACIAL-PARESTHESIA TIME). As far as the author knows, this method has not been tried in cardiac catheterization There appears to be unjustifiable fear associated with the intracardiac injection of ether In the author's judgment, injection of minute amounts of ether carries with it no significant risk. The appearance of paresthesias following such an injection would help to differentiate promptly between an interatrial and an interventricular septal defect with pulmonic stenosis For this purpose, the author recommends the injection of 2 to 3 minims ether mixed with 3 to 5 ml saline This could be rapidly injected into the heart after the catheter has been placed below the tricuspid orifice. Although the mere appearance of paresthesias would serve as the diagnostic indicator for the presence of a right-to-left shunt at the ventricular level, the time elapsing between the injection and the onset of facial paresthesias could also be measured

The ether method could therefore be employed as a qualitative and quantitative test during cardiac catheterization for the diagnosis of a ventricular defect with an overriding aorta, conversely, the absence of a right-to-left shunt below the tricuspid orifice. Based on a long experience with the conventional ether method, the author believes that the values obtained should compare well with those obtained with fluorescein, Evans blue, or indigo carmine.

Objective Method for Diagnosis of Left-to-right Shunts. Braunwald et al. employed a technique which makes possible the precise localization of left-to-right shunts A dye indicator, Evans blue or indigo carmine, was rapidly injected into chambers of the left heart or aorta via left heart catheterization When the dye indicator was rapidly injected and the dilution curve was recorded from a peripheral artery (femoral or ulnar) by means of a cuvette densitometer, a characteristic dye dilution curve was obtained (Part 4, Chap 6). Through this technique, differentiation could be made between (1) ventricular septal defect and aortic septal defect, (2) aortic septal defect and patent ductus arteriosus

In other congenital heart diseases associated with enlargement of both atria, the tall P waves become also broad (0.12 sec or more in lead II) and diphasic, with a predominant negative phase in V_1 to V_2. These signs of biatrial enlargement are found in (1) atrial septal defect, (2) AV communis, (3) tricuspid atresia

In tricuspid atresia, the broad and diphasic P wave has the peculiarity that in several leads, the first phase (due to the electrical forces of the right atrium) is greater than the second (due to the electrical forces of the left atrium).

P-R Interval. Lengthening of the P-R interval above 0.20 sec in lead II (*first-degree AV block*) is observed in (1) atrial septal defect, (2) ventricular septal defect, (3) Ebstein's disease, (4) patent ductus arteriosus Second and third (complete) degree of AV block may also be present in congenital heart disease. *Complete AV block* is not necessarily associated with ventricular septal defect, as erroneously believed in the past.

QRS Complex and T Wave. The determination of the *mean manifest electrical axes* of the QRS complex and the T wave (ÂQRS and

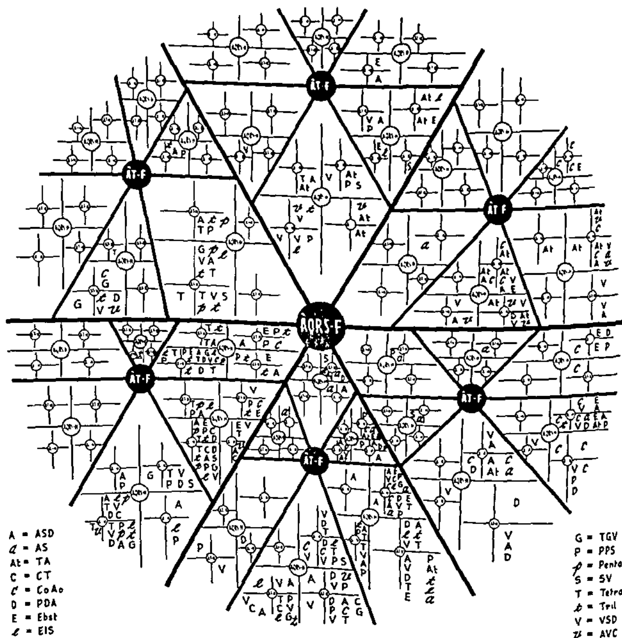


Fig. 6-18. Table-diagram for the combined frontal and horizontal representation of ÂQRS and ÂT for the electrocardiographic classification of congenital heart lesions. (See text for key to symbols.) (*Courtesy of the American Heart Journal; Ayala y De Landero Am Heart J., 1959.*)

5

The electrocardiogram in congenital heart disease

DEMETRIO SODI PALLARES
AND MARIO R. TESTELLI

Many treatises of congenital heart disease and textbooks of electrocardiography do not sufficiently stress that *the electrocardiogram is an important aid for the diagnosis of congenital heart disease.* In the authors' opinion, when the electrocardiogram is "understood" in relation to the activation process, certain "patterns" acquire a significance that is specific for certain groups of congenital malformations of the heart or even for individual entities Specifically, through the electrocardiographic diagnosis of *enlargement* (hypertrophy or dilatation) of one or more cardiac chambers and of *myocardial damage* (ischemia or injury), hemodynamic alterations can be recognized with a good degree of accuracy. Once these alterations are recognized, the main diagnostic possibilities can be suggested

GENERAL APPROACH TO ELECTROCARDIOGRAPHY

Before giving a description of the more frequent "patterns" that are encountered in the various forms of congenital heart disease, the approach to electrocardiography in congenital heart disease that is followed at the National Institute of Cardiology of Mexico will be briefly outlined (Sodi Pallares).

P Wave. In some congenital heart diseases, characteristic alterations of the P wave (the "P congenitale" of Zuckermann et al) are observed. peaked and tall P waves (3 mm or more), which are usually of normal duration in leads I, II, aVF, and aVL; the AP is around +30°. In the right precordial leads (V_1 to V_2), the P wave is positive or sharply diphasic with a predominantly positive phase.

The *P congenitale* is frequently found in the following conditions. (1) isolated or pure pulmonary stenosis (trilogy, tetralogy, pentalogy), (2) "complicated" pulmonary stenosis, (3) transposition of the great vessels, (4) common trunk, (5) AV communis (total or partial), (6) Ebstein's disease, (7) tricuspid stenosis (congenital or acquired)

In Ebstein's disease and tricuspid stenosis, a special type of P congenitale is encountered: the voltage of the P wave can be greater than that of the QRS complex in V_1 to V_2 (*giant P wave*)

Although the degree of cyanosis may be important, the P congenitale is thought to be due to *enlargement of the right atrium in hearts with horizontal electrical position.* It is worth pointing out the great similarity in pattern between the P congenitale and the "P pulmonale" that is typically found in chronic cor pulmonale The only difference is that the AP of the P pulmonale is located around +80° (P wave tall and peaked in leads II, III, and aVF) as a result of *increased electrical forces of the enlarged right atrium in hearts with vertical electrical position.* The similarity between the P congenitale and the P pulmonale is, then, easily understood, since both are fundamentally due to the same mechanism (right atrial enlargement), the latter when the heart is vertical, the former when the heart is horizontal

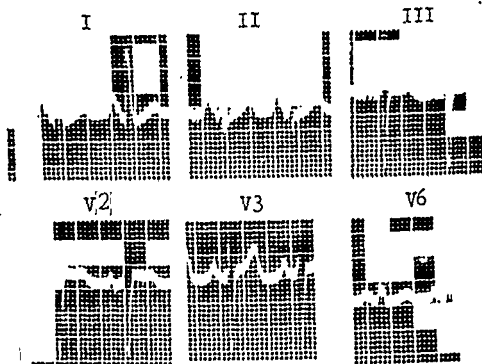


Fig. 6-20. Electrocardiogram of a patient with tricuspid atresia. (This and all subsequent electrocardiograms were taken with normal standardization for the limb leads and with N/2 standardization for the precordial leads.) (Courtesy of the *American Heart Journal.*)

tions are not included). Like any other table that might be suggested, it is a simple aid intended to orient the clinician. The next and necessary step is to study the entire electrocardiogram in function of the activation process (see Part 2, Chap. 37, Epicardial and Endocardial Electrocardiograms).

PATTERNS OF CONGENITAL HEART DISEASE IN THE CHEST LEADS

In order to facilitate the understanding of the electrocardiogram in the various congenital heart diseases, a brief review of the most important unipolar QRS patterns recorded by the precordial leads will be made

Tall R Wave in V_1 to V_2. The normal pattern in V_1 to V_2 is rS with negative T wave up to about 15 years of age The R wave in V_1 to V_2 is considered tall when the ratio R/S or R/q is greater than 1 or when the ratio R/R + S is greater than 0 5. The electrocardiograms of children under the age of 3 years should be excluded because ratios greater than 1 or 0.5, respectively, frequently correspond to hearts that are clinically and radiologically normal.

A tall R wave in V_1 to V_2 can be found with ventricular complexes of the following types: *R wave with or without initial slurring, Rs, qR, qRs, or rR* (Fig. 6-21A). This pattern in V_1 to V_2 is characteristic of *right ventricular hypertrophy* (anatomic diagnosis) and *right ventricular systolic overload* (hemodynamic correlation).[1] The pattern is encountered in 10 congenital and, less frequently, in 3 acquired heart diseases.

1 Isolated pulmonary stenosis
2 "Complicated" pulmonary stenosis (trilogy, tetralogy, or pentalogy)
3 Idiopathic or essential pulmonary hypertension
4 Patent ductus arteriosus } with marked
5. Ventricular septal defect } pulmonary
6 Atrial septal defect } hypertension
7 Eisenmenger complex
8 AV communis (total or partial)
9. Common trunk
10. Transposition of the great vessels
a Mitral valve disease (stenosis, insufficiency, or both)
b Chronic cor pulmonale

[1] Ventricular systolic overload, according to Cabrera and Monroy (1952a and b), is the result of an increase of the mean systolic pressure within the ventricle, which may or may not be associated with hypertension in the corresponding artery (aorta for the left ventricle, and pulmonary artery for the right ventricle).

ÂT) in the frontal and horizontal planes has proved to be useful for the diagnosis of uncomplicated congenital heart diseases (Ayala y De Landero et al.). Figure 6-18 represents an extension of *Bayley's triaxial system* to which a four-quadrant system for the horizontal plane has been added.

KEY TO SYMBOLS FOR CONGENITAL CARDIAC MALFORMATIONS

Congenital malformation	*Abbreviations*	*Abbreviations used in Fig 6-18*
Aortic stenosis	A S	a
Atrial septal defect	A S D	A
Atrioventricularis communis	A V C.	v
Coarctation of the aorta	Co Ao.	c
Common trunk	C.T	C
Ebstein's disease	Ebst	E
Eisenmenger's complex	EIS	e
Patent ductus arteriosus	P D A	D
Pentalogy of Fallot	Penta	p
Pure pulmonary stenosis	P P S	P
Single ventricle	S V	S
Tetralogy of Fallot	Tetra	T
Transposition of the great vessels	T G V	G
Tricuspid atresia	T A	At
Trilogy of Fallot	Tril	t
Ventricular septal defect	V S D	V

The use of the table may be summarized as follows

1 *The large triaxial system* (ÂQRS-F) divides the *frontal* planes in six large *sextants* (ÂT-F) *The first stage then* consists of localizing the ÂQRS in one of the six large sextants

2 Within each large sextant there is a smaller triaxial system emanating from the black ÂT-F, which serves to localize *the* ÂT in the frontal *plane*

3 Within each of the 36 frontal ÂT sextants are *four large* quadrants emanating from a white circle labeled *ÂQRS-H*, which are used for the determination of ÂQRS in the horizontal plane according to the scheme of Fig 6-18.

4 Within each of the 144 horizontal QRS quadrants are four smaller quadrants emanating from white circles, labeled ÂT-H, which *serve* to *localize the* ÂT in the horizontal plane according to the same scheme of Fig 6-19

Once these four *steps* are *followed*, any electrocardiogram can be quickly localized in any of the 576 small quadrants of Fig. 6-18 Within these quadrants are inscribed, in *order* of frequency,

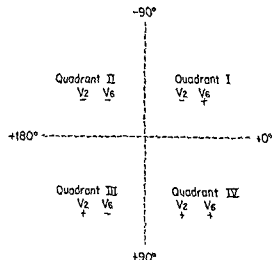


Fig. 6-19. The four quadrants in the horizontal plane (seen from above) determined by the positive (+) and negative (−) areas of the QRS complex and T wave in leads V_2 and V_6. (*Courtesy of the American Heart Journal*)

the symbols corresponding to the congenital heart diseases which present that particular localization of ÂQRS and ÂT *in the frontal* and *horizontal* planes. The symbols are explained in the annexed table (Ayala y De Landero et al).

An example will serve to illustrate how to use this method *in the study* of congenital heart disease. In the electrocardiogram of Fig 6-19, the ÂQRS in the frontal plane is −30°, i e , it falls in the first large sextant, and ÂT is +50°, which falls in the sixth small sextant (comprised in the first *large sextant*) Next, the horizontal ÂQRS and ÂT *are* considered According to the scheme of *Fig* 6-18, *the* ÂQRS in the horizontal plane (ÂQRS-H) is localized in the first large quadrant and the ÂT in the fourth smaller ÂT-H quadrant. *In summary, the* electrocardiogram under study (Fig. 6-19) is localized as follows. ÂQRS-F (first *large* sextant), ÂT-F (sixth *small sextant*), ÂQRS-H (first large quadrant), and *ÂT-H (fourth small* quadrant) ...

symbol

sociate

and Â?

tion of the aorta C, atrial septal defect *A*, ventricular septal defect V, aortic stenosis *a*, and AV communis c. In the electrocardiogram under discussion, the diagnosis *proved* to be tricuspid *atresia*

The table shown with Fig. 6-18 helps to orient the *diagnosis* toward the *most* common *possibilities* in the field of congenital heart disease (complex anomalies and rare malforma-

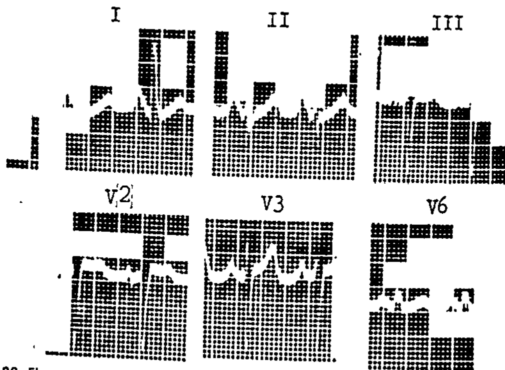


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A tall R wave in V_1 to V_2 can be found with ventricular complexes of the following types. *R wave with or without initial slurring, Rs, qR, qRs, or rR* (Fig 6-21A). This pattern in V_1 to V_2 is characteristic of *right ventricular hypertrophy* (anatomic diagnosis) and *right ventricular systolic overload* (hemodynamic correlation)[1] The pattern is encountered in 10 congenital and, less frequently, in 3 acquired heart diseases

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6. Atrial septal defect } hypertension
7. Eisenmenger complex
8. AV communis (total or partial)
9. Common trunk
10. Transposition of the great vessels
    a Mitral valve disease (stenosis, insufficiency, or both)
    b Chronic cor pulmonale

[1] Ventricular systolic overload, according to Cabrera and Monroy (1952a and b), is the result of an increase of the mean systolic pressure within the ventricle, which may or may not be associated with hypertension in the corresponding artery (aorta for the left ventricle, and pulmonary artery for the right ventricle).

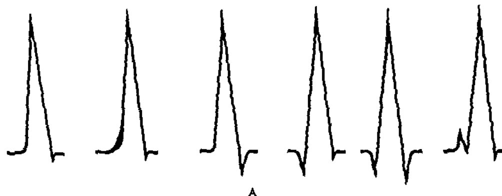


Fig 6-21A. The pattern of tall R wave in leads V_1 to V_2 (R with or without initial slurring, Rs, qR, qRs, or rR) characteristic of right ventricular hypertrophy, which can be found in 10 congenital and, less frequently, in 3 acquired heart diseases According to the form of the T wave (positive, diphasic, or negative) in the same leads, three subgroups of congenital heart diseases can be considered (see text).

c. Fibrocystic disease of the pancreas (mucoviscidosis)

It should be said that in correspondence with a tall R wave in V_1 to V_2, tall, isodiphasic complexes are recorded in the "transitional leads" (V_3 to V_4). In the opinion of the authors, these complexes should be interpreted as the potential variations of the hypertrophied, low right septal mass. In the absence of left ventricular hypertrophy, rS is also recorded in V_5 to V_6.

If the form of the T wave in the same leads is considered and the acquired heart diseases are excluded, the diagnostic possibilities are reduced, and three subgroups can be considered

TALL R WAVE WITH POSITIVE T WAVE IN V_1 TO V_2. *Acyanotic Heart Diseases*

1 Ventricular septal defect
2. Isolated pulmonary stenosis
3 Patent ductus arteriosus

Cyanotic Heart Diseases

1. Tetralogy of Fallot
2 Transposition of the great vessels
3. Common trunk

TALL R WAVE WITH DIPHASIC T WAVE IN V_1 TO V_2 (*negative T wave with terminal positivity preceded by sagging and upward convexity of the RS-T segment*) This pattern can be found in the same two groups above. However, the value of right ventricular or pulmonary artery pressure is comparatively greater for the same disease when the pattern of tall R wave in V_1 to V_2 is accompanied by a diphasic T wave than when it is accompanied by a positive T wave.[2]

TALL R WAVE WITH NEGATIVE T WAVE IN V_1 TO V_2. When a tall R wave in the right precordial leads is followed by a negative T wave of the ischemic type (symmetric), the degree of right ventricular hypertrophy (and systolic overload) is extreme. The right ventricular systolic pressure is equal to or higher than the left ventricular systolic pressure, and the disease has reached the final stage of its natural evolution

In order of frequency, this pattern is seen in (1) isolated pulmonary stenosis, (2) trilogy of Fallot, (3) idiopathic or essential pulmonary hypertension, (4) Eisenmenger complex, (5) patent ductus arteriosus (few cases), (6) atrial septal defect (few cases).

It should be appreciated that the pattern of tall R wave in V_1 to V_2 in congenital heart disease acquires its main diagnostic significance when it is considered in conjunction with the T-wave changes in the same leads. With increasing pressure inside the right ventricle, the

[2] It is evident that any electrocardiographic pattern must be evaluated in relation to the specific *congenital heart disease in which it is encountered.* Thus the hemodynamic significance of a given pattern [illegible] This [illegible] in- [illegible] Hg [illegible] very high in atrial septal defect, and *moderate* in pure pulmonary stenosis.

T wave changes from positive to diphasic, and finally becomes negative. By analogy to what has been found in experimental coronary occlusion and in clinical coronary heart disease, the T-wave changes in congenital heart disease are interpreted to indicate (1) subendocardial ischemia of the free right ventricular wall (positive T wave in V_1 to V_2); (2) progressive myocardial ischemia (diphasic T wave in V_1 to V_2); (3) subepicardial ischemia (negative T wave in V_1 to V_2).

rS Complex with Positive T Wave in V_1 to V_2. It is commonly accepted that a ventricular complex of the rS type (with an r/S ratio greater than 1:10) in the right precordial leads indicates *left ventricular hypertrophy*, the S wave being due to the electrical forces of the hypertrophied left ventricle pointing toward the left and backwards However, it is not sufficiently known that the same pattern may be observed in cases of *right ventricular hypertrophy*, more precisely of hypertrophy of the basal portions (*crista supraventricularis*) of the right ventricle. In such cases, the rS complex with positive T wave in V_1 to V_2 represents the potential variations transmitted from the trabecular zone of the right ventricle When it is doubtful whether the rS complex in V_1 to V_2 indicates left or right ventricular hypertrophy, the differential diagnosis can be made by considering the pattern of lead aVR: in right ventricular hypertrophy, there is a qR shape with late and tall R wave; in left ventricular hypertrophy, there is a Qr pattern.

rS Complex with Positive T Wave in V_1 to V_2—Indicative of Right Ventricular Hypertrophy (RVH). This is found in (1) tetralogy of Fallot,[3] (2) transposition of the great vessels.

rS Complex with Positive T Wave in V_1 to V_2—Indicative of Left Ventricular Hypertrophy (LVH). This is found in (1) tricuspid atresia, (2) aortic or subaortic stenosis, (3) coarctation of the aorta

rsR' Complex in V_1 to V_2. Certain electrocardiograms show a tall and late R wave (complexes of the rsR' or rsR'S' type) in the right precordial leads while qRS complexes with slurred S wave are observed in the left precordial leads (Fig. 6-21B, *A*). Studies of "direct" electrocardiography in dog and man have demonstrated that in uncomplicated right bundle branch block (RBBB), the patterns recorded in V_1 to V_2 are due to transmission of the potential variations of the free right ventricular wall, those of V_3 are due to the trabecular zone of the right ventricle, those of V_4 are due to the right septal mass, and those of V_5 to V_6 are due to the free left ventricular wall On the basis of these observations, a diagnosis of right ventricular enlargement (dilatation or hypertrophy) is made when right ventricular patterns are recorded up to V_5 to V_6 (Fig 6-21B, *B*). When the pattern of the right atrium (in the absence of myocardial infarction) is recorded in V_1 to V_2 and a right ventricular pattern is recorded in the other precordial leads (Fig. 6-21B, *C*), *right ventricular and right atrial enlargement* is diagnosed. If the pattern of the right atrium is recorded in several precordial leads (Fig. 6-21B, *D*), a *giant right atrium* is present. When increased voltage of the positive deflections (with the pattern of RBBB) is recorded in V_3 and V_4, hypertrophy of the right septal mass and (by deduction) of the entire right ventricle is diagnosed (Fig. 6-21B, *E*). Following the same line of reasoning, it is not surprising that *left ventricular hypertrophy can be diagnosed in the presence of RBBB* when left ventricular patterns are recorded from V_3 to V_6 (Fig. 6-21B, *F*). In the same way, *left ventricular hypertrophy and right atrial enlargement* are diagnosed when, in addition to the fact that left ventricular patterns are already recorded in V_3, the pattern of the right atrium is recorded in leads V_1 to V_2 (Fig 6-21B, *G*).

The pattern of RBBB with characteristic variations (see below) is encountered in the following diseases. (1) atrial septal defect, (2) ventricular septal defect, (3) AV communis (with AQRS deviated to the left), (4) ostium primum (with AQRS deviated to the left), (5) Eisenmenger complex, (6) Ebstein's disease.

QS Pattern with Positive T Wave in V_1 to V_2. In the absence of myocardial infarction, a QS pattern with positive T wave in V_1 to V_2 is indicative of *left bundle branch block* (usually accompanied by LVH and systolic overload) and is associated with characteristic patterns in leads V_5 to V_6. Depending on the degree of the LBBB, the left precordial leads may show

[3] It should not cause surprise that the electrocardiogram in the tetralogy of Fallot may present a tall R wave or an rS complex with positive T wave in V_1 to V_2 This depends on the degree and location of the hypertrophy of the right ventricle

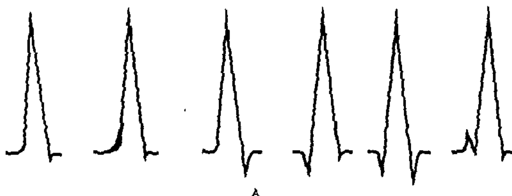


Fig 6-21A The pattern of tall R wave in leads V_1 to V_2 (R with or without initial slurring, Rs, qR, qRs, or rR) characteristic of right ventricular hypertrophy, which can be found in 10 congenital and, less frequently, in 3 acquired heart diseases. According to the form of the T wave (positive, diphasic, or negative) in the same leads, three subgroups of congenital heart diseases can be considered (see text)

c. Fibrocystic disease of the pancreas (mucoviscidosis)

It should be said that in correspondence with a tall R wave in V_1 to V_2, tall, isodiphasic complexes are recorded in the "transitional leads" (V_3 to V_4). In the opinion of the authors, these complexes should be interpreted as the potential variations of the hypertrophied, low right septal mass. In the absence of left ventricular hypertrophy, rS is also recorded in V_5 to V_6.

If the form of the T wave in the same leads is considered and the acquired heart diseases are excluded, the diagnostic possibilities are reduced, and three subgroups can be considered.

TALL R WAVE WITH POSITIVE T WAVE IN V_1 TO V_2 *Acyanotic Heart Diseases*

1. Ventricular septal defect
2. Isolated pulmonary stenosis
3. Patent ductus arteriosus

Cyanotic Heart Diseases

1. Tetralogy of Fallot
2. Transposition of the great vessels
3. Common trunk

TALL R WAVE WITH DIPHASIC T WAVE IN V_1 TO V_2 (*negative T wave with terminal positivity preceded by sagging and upward convexity of the RS-T segment*). This pattern can be found in the same two groups above. However, the value of right ventricular or pulmonary artery pressure is comparatively greater for the same disease when the pattern of tall R wave in V_1 to V_2 *is* accompanied by a diphasic *T* wave than when it *is* accompanied by a positive T wave.[2]

TALL R WAVE WITH NEGATIVE T WAVE IN V_1 TO V_2 When a tall R wave in the right precordial leads is followed by a negative T wave of the ischemic type (symmetric), the degree of right ventricular hypertrophy (and systolic overload) is extreme. *The right ventricular systolic pressure is equal to or higher than the left ventricular systolic pressure, and the disease has reached the final stage of its natural evolution.*

In order of frequency, this pattern is seen in (1) isolated pulmonary stenosis, (2) trilogy of Fallot, (3) idiopathic or *essential pulmonary hypertension,* (4) Eisenmenger complex, (5) patent *ductus arteriosus (few cases),* (6) atrial septal *defect (few cases).*

It should be appreciated that *the pattern of* tall R wave in V_1 to V_2 in congenital heart disease acquires its main diagnostic significance *when it is considered in conjunction* with the T-wave changes *in the same* leads With increasing pressure inside *the right* ventricle, the

[2] *It is evident that any electrocardiographic pattern must be evaluated in relation to the specific congenital heart* disease in which it is encountered *Thus the hemodynamic significance* of a given pattern may vary according to the *circumstances* This is also true of certain hemodynamic data. *For instance, a right ventricular* pressure of 80 mm Hg is considered very *high in atrial* septal defect, and moderate *in pure pulmonary* stenosis.

T wave changes from positive to diphasic, and finally becomes negative. By analogy to what has been found in experimental coronary occlusion and in clinical coronary heart disease, the T-wave changes in congenital heart disease are interpreted to indicate (1) subendocardial ischemia of the free right ventricular wall (positive T wave in V_1 to V_2), (2) progressive myocardial ischemia (diphasic T wave in V_1 to V_2); (3) subepicardial ischemia (negative T wave in V_1 to V_2).

rS Complex with Positive T Wave in V_1 to V_2. It is commonly accepted that a ventricular complex of the rS type (with an r/S ratio greater than 1:10) in the right precordial leads indicates *left ventricular hypertrophy,* the S wave being due to the electrical forces of the hypertrophied left ventricle pointing toward the left and backwards. However, it is not sufficiently known that the same pattern may be observed in cases of *right ventricular hypertrophy,* more precisely of hypertrophy of the basal portions (*crista supraventricularis*) of the right ventricle. In such cases, the rS complex with positive T wave in V_1 to V_2 represents the potential variations transmitted from the trabecular zone of the right ventricle. When it is doubtful whether the rS complex in V_1 to V_2 indicates left or right ventricular hypertrophy, the differential diagnosis can be made by considering the pattern of lead aVR. in right ventricular hypertrophy, there is a qR shape with late and tall R wave, in left ventricular hypertrophy, there is a Qr pattern.

rS Complex with Positive T Wave in V_1 to V_2—Indicative of Right Ventricular Hypertrophy (RVH). This is found in (1) tetralogy of Fallot,[3] (2) transposition of the great vessels.

rS Complex with Positive T Wave in V_1 to V_2—Indicative of Left Ventricular Hypertrophy (LVH). This is found in (1) tricuspid atresia, (2) aortic or subaortic stenosis, (3) coarctation of the aorta

rsR′ Complex in V_1 to V_2. Certain electrocardiograms show a tall and late R wave (complexes of the rsR′ or rsR′S′ type) in the right precordial leads while qRS complexes with slurred S wave are observed in the left precordial leads (Fig. 6-21B, *A*). Studies of "direct" electrocardiography in dog and man have demonstrated that in uncomplicated right bundle branch block (RBBB), the patterns recorded in V_1 to V_2 are due to transmission of the potential variations of the free right ventricular wall, those of V_3 are due to the trabecular zone of the right ventricle, those of V_4 are due to the right septal mass, and those of V_5 to V_6 are due to the free left ventricular wall. On the basis of these observations, a diagnosis of right ventricular enlargement (dilatation or hypertrophy) is made when right ventricular patterns are recorded up to V_5 to V_6 (Fig 6-21B, *B*). When the pattern of the right atrium (in the absence of myocardial infarction) is recorded in V_1 to V_2 and a right ventricular pattern is recorded in the other precordial leads (Fig. 6-21B, *C*), *right ventricular and right atrial enlargement* is diagnosed. If the pattern of the right atrium is recorded in several precordial leads (Fig. 6-21B, *D*), a *giant right atrium* is present. When increased voltage of the positive deflections (with the pattern of RBBB) is recorded in V_3 and V_4, hypertrophy of the right septal mass and (by deduction) of the entire right ventricle is diagnosed (Fig 6-21B, *E*). Following the same line of reasoning, it is not surprising that *left ventricular hypertrophy can be diagnosed in the presence of RBBB* when left ventricular patterns are recorded from V_1 to V_6 (Fig. 6-21B, *F*). In the same way, *left ventricular hypertrophy and right atrial enlargement* are diagnosed when, in addition to the fact that left ventricular patterns are already recorded in V_3, the pattern of the right atrium is recorded in leads V_1 to V_2 (Fig 6-21B, G)

The pattern of RBBB with characteristic variations (see below) is encountered in the following diseases (1) atrial septal defect, (2) ventricular septal defect, (3) AV communis (with ÂQRS deviated to the left), (4) ostium primum (with ÂQRS deviated to the left), (5) Eisenmenger complex, (6) Ebstein's disease

QS Pattern with Positive T Wave in V_1 to V_2. In the absence of myocardial infarction, a QS pattern with positive T wave in V_1 to V_2 is indicative of *left bundle branch block* (usually accompanied by LVH and systolic overload) and is associated with characteristic patterns in leads V_5 to V_6 Depending on the degree of the LBBB, the left precordial leads may show

[3] It should not cause surprise that the electrocardiogram in the tetralogy of Fallot may present a tall R wave or an rS complex with positive T wave in V_1 to V_2 This depends on the degree and location of the hypertrophy of the right ventricle

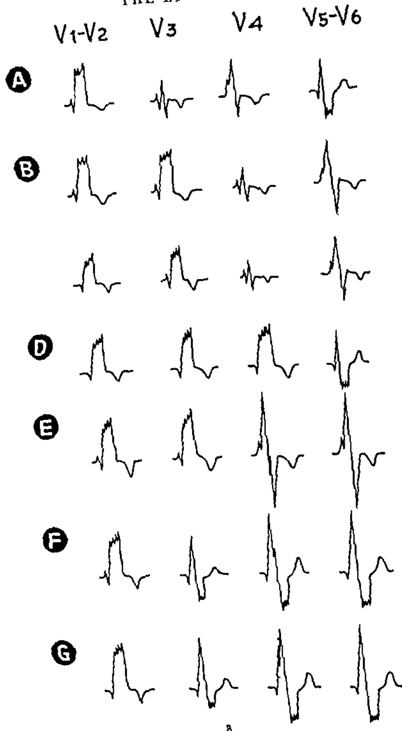


Fig 6-21B. Patterns of ventricular and/or atrial enlargements (dilatation or hypertrophy) in the presence of RBBB A. Uncomplicated RBBB. B RBBB with right ventricular enlargement C. RBBB with right ventricular and right atrial enlargement. D RBBB with giant right atrium. E. RBBB with right ventricular hypertrophy (right septal mass). F. RBBB with left ventricular hypertrophy. G. RBBB with left ventricular hypertrophy and right atrial enlargement

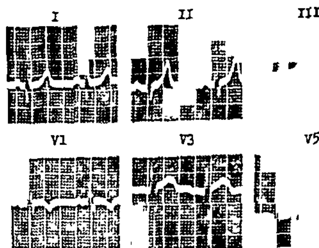


Fig. 6-22. Ventricular septal defect. In V_1 the morphology is "M"-shaped, with the first positivity (R) greater than the second (R'). The deep Q wave in V_5 and the tall R wave in V_1 are interpreted to indicate left septal hypertrophy.

only absence of the normal q wave (first degree), an initial slurring of the R wave with or without rounded peak (second degree), or an M pattern (third, or advanced, degree).

The patterns of LBBB are found in (1) aortic stenosis, (2) tricuspid atresia, (3) coarctation of the aorta, (4) patent ductus arteriosus

Tall R Wave in V_1 to V_2 and in V_5 to V_6. Under this heading are included the electrocardiograms showing "true" biventricular hypertrophy. As a tall R wave in V_5 to V_6 not too infrequently can correspond to the potential variations of the hypertrophied and dilated right cardiac chambers, one should be certain that the tall R wave in V_5 to V_6 represents the transmission of the potential variations of the associated hypertrophied left ventricle To this purpose, one should pay attention to three data that confirm the presence of associated hypertrophy: (1) initial q wave in V_5 to V_6, (2) delayed intrinsicoid deflection in V_5 to V_6, (3) the transitional complexes of V_3 to V_4 are followed by complexes of the qR type (not rS) in V_5 to V_6

The pattern of biventricular hypertrophy frequently corresponds to a systolic overload of the right ventricle associated with a diastolic overload [4] of the left (tall, positive T wave in V_5 to V_6, in addition to the tall R wave in the same leads). This pattern is usually seen in

[4] The term "ventricular diastolic overload," according to Cabrera and Monroy (1952a and b), means that one ventricle receives (in diastole) and ejects (in systole) a greater volume of blood than the other ventricle.

1. *Acyanotic heart diseases*
   a. Patent ductus arteriosus
   b. Ventricular septal defect
2. *Cyanotic heart diseases*
   a Pentalogy of Fallot
   b Tricuspid atresia
   c. Common trunk
   d. AV communis

After this outline of the authors' approach to electrocardiography in congenital heart disease, the most representative patterns of the main malformations will be reviewed.

ELECTROCARDIOGRAPHIC PATTERNS OF THE MOST IMPORTANT MALFORMATIONS

Ventricular Septal Defect

1. *Signs of RVH with some degree of RBBB.*
   a In V_1 to V_2, the first R wave is frequently greater than the second (R') and the T wave is frequently positive (Fig 6-22).
   b V_3 to V_4 show large isodiphasic complexes with positive T waves [Fig 6-22(1)].
2. *Signs of LVH.*
   a In V_5 to V_6, tall R complexes (of the type qRs or qRS) are present, followed by positive and tall (symmetric) T waves This pattern of LVH is usually accompanied by diastolic overload of the left ventricle with a relatively low right ventricular pressure (not exceeding 60 mm Hg) [Fig. 6-22(1)].
   b. In V_5 to V_6, deep and rapid Q waves

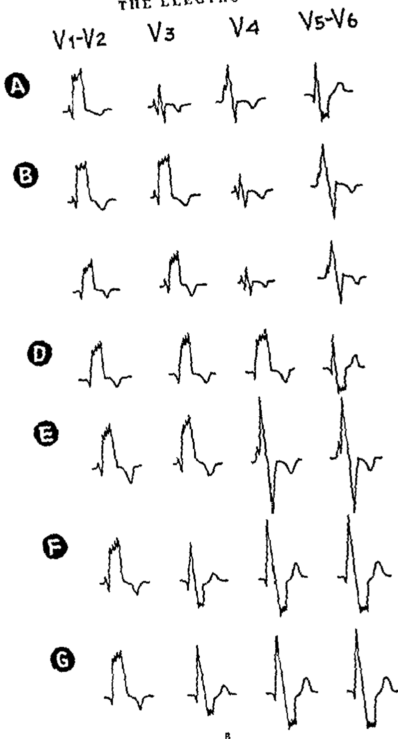


Fig. 6-218. Patterns of ventricular and/or atrial enlargements (dilatation or hypertrophy) in the presence of RBBB. A. *Uncomplicated* RBBB. B. RBBB with right ventricular enlargement. C. RBBB with right ventricular and right atrial *enlargement*. D. RBBB with giant right atrium. E. RBBB with right ventricular hypertrophy (right septal mass). F. RBBB with *left ventricular* hypertrophy. G. RBBB with left ventricular hypertrophy and right atrial enlargement.

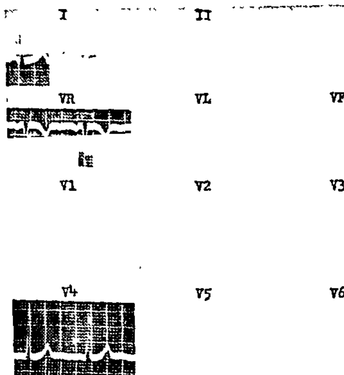


Fig. 6-22(2). Patent ductus arteriosus without pulmonary hypertension. Tall R waves with an upward concavity of the RS-T segment, and positive and peaked T waves are inscribed from V_4 through V_6.

Pure Pulmonary Stenosis

Pure pulmonary stenosis is another malformation in which the electrocardiogram closely correlates with the hemodynamic alterations

1. *Mild degree of stenosis* The electrocardiogram [Fig. 6-22(5)] may be of the type S1-S2-S3 with small isodiphasic complexes in the precordial leads and "normal" R/S or R/S + R ratios in V_1, and minor changes of the P waves (slightly peaked in lead 1 and V_1 with ÂP deviated to the left).

2. *Severe degree of stenosis.* The electrocardiogram becomes more characteristic of RVH [Fig. 6-22(6)]. The T waves in the right precordial leads are usually positive when the right ventricular systolic pressure is lower than the systemic. However, when that pressure is equal to or higher than the systemic, the T waves in the right and then in most precordial leads become negative of the "ischemic type" As discussed earlier, such a pattern is indicative of "extreme" RVH (and systolic overload), a pattern which is more typical of the *trilogy of Fallot* [Fig. 6-22(13)]

Eisenmenger Complex

1. *Signs of RVH with RBBB.*

a. The pattern of the right ventricle (rsR' or rsR'S') is recorded in various precordial leads [Fig. 6-22(7)].

b. Large isodiphasic complexes are seen in the intermediate precordial leads (as in ventricular septal defect); the pattern of the right septal mass (RS) is recorded in V_5 to V_6.

2. *Signs of hypertrophy of the left septal mass* and (by deduction) *of the left ventricle.*

a. Deep and rapid Q wave (less than 0 04 sec) is recorded in leads, reflecting the potential variations of the left ventricle (as in ventricular septal defect).

Tricuspid Atresia

1 The P wave in the standard leads is tall, broad, and notched, the first peak being greater than the second (Fig. 6-20). In the right precordial leads, the P wave is diphasic, with an important positive phase.

2. *Signs of LVH with LBBB.*

a ÂQRS deviated to the left. It is classically admitted that the association of *left axis deviation* with *cyanosis* is highly suggestive of tricuspid atresia.

b There is an rS complex in V_1 to V_2, and a tall R wave is present in V_5 to V_6.

AV Communis (Total or Partial)

1. Evidence of biventricular hypertrophy with RBBB and *left axis deviation* [Fig. 6-22(8)].

a Tall R' in V_1 to V_2 (hypertrophy of the

(less than 0.04 sec) are present, synchronous with the first tall R wave in V_1 to V_2. This fact should be interpreted as evidence of hypertrophy of the interventricular septum, where ventricular activation normally starts (middle third of the left septal mass) (Fig. 6-22).

3 The same patterns of V_5 to V_6 are often recorded also in leads II, III, and aVF.

Patent Ductus Arteriosus

1. The P wave may be broad and slurred, with a duration of 0 12 sec or more in the standard leads

2. There is evidence of RVH with systolic overload.

a. V_1 to V_2 present tall R waves with negative T waves

b. V_3 to V_4 show large isodiphasic complexes with positive or diphasic T waves.

3 There is evidence of LVH with diastolic overload

In V_5 to V_6 there are tall R waves with positive T waves When only these signs are present, the pulmonary pressure is not greatly elevated [Fig. 6-22(2)]. however, when these signs are associated with those of RVH, pulmonary hypertension is present [Fig. 6-22(3)]. Sometimes it is impossible to differentiate the pattern of ventricular septal defect from that of patent ductus arteriosus. It may be of help to remember that the T wave in V_1 to V_2 is frequently positive in ventricular septal defect and diphasic or negative in patent ductus arteriosus

Atrial Septal Defect

1. The P wave in the standard leads is frequently broad (*left atrial enlargement*). Signs of *right atrial enlargement* (high and peaked P wave mainly in leads I and II) may also be *present*.

2. *First-degree AV block.*

3. *Complete or incomplete RBBB* [Fig. 6-22(4)].

It is important to know that as the pulmonary hypertension increases, the following modifications are seen:

1. The patterns of leads V_3 to V_4 show an increase in voltage and are "displaced" to the left.

2. The patterns of V_1 to V_2 show more typical evidence of RVH, however, the presence of RBBB is revealed by the initial slurring of the R wave (this is interpreted differently by some authors).

I II III

VR VL VF

V1 V2 V3

V4 V5 V6

Fig 6-22(1) Ventricular septal defect. Signs of left ventricular hypertrophy with diastolic overloading. Note large isodiphasic complexes in leads V_3 to V_4.

3 The T waves become more negative and of the "ischemic" type in all leads

In summary, the natural evolution of the electrocardiogram in atrial septal defect[5] is toward a pattern of systolic overload of the right ventricle, which is progressively reached.

[5] In the natural history of atrial septal defect it is reported that primary pulmonary hypertension is frequently found This would be in accordance with the electrocardiographic evolution, since the electrocardiogram of atrial septal defect with marked pulmonary hypertension cannot be differentiated from that of primary pulmonary hypertension

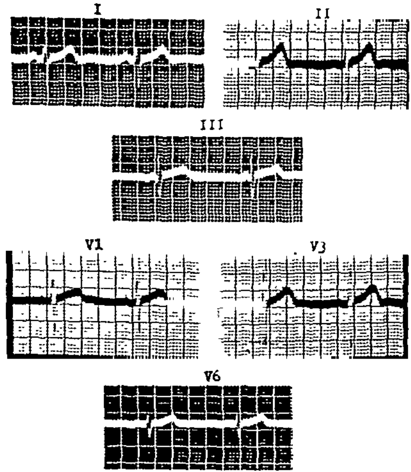


Fig. 6-22(5). Pure pulmonary stenosis. Electrocardiogram of the type S_1-S_2-S_3.

(less than 0.04 sec) are present, synchronous with the first tall R wave in V_1 to V_2. This fact should be interpreted as evidence of hypertrophy of the interventricular septum, where ventricular activation normally starts (middle third of the left septal mass) (Fig 6-22).

3. The same patterns of V_5 to V_6 are often recorded also in leads II, III, and aVF.

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1. The P wave may be broad and slurred, with a duration of 0 12 sec or more in the standard leads.

2. There is evidence of RVH with systolic overload

a V_1 to V_2 present tall R waves with negative T waves

b. V_3 to V_4 show large isodiphasic complexes with positive or diphasic T waves

3. There is evidence of LVH with diastolic overload.

In V_5 to V_6 there are tall R waves with positive T waves When only these signs are present, the pulmonary pressure is not greatly elevated [Fig 6-22(2)]: however, when these signs are associated with those of RVH, pulmonary hypertension is present [Fig 6-22(3)] Sometimes it is impossible to differentiate the pattern of ventricular septal defect from that of patent ductus arteriosus It may be of help to remember that the T wave in V_1 to V_2 is frequently positive in ventricular septal defect and diphasic or negative in patent ductus arteriosus.

Atrial Septal Defect

1. The P wave in the standard leads is frequently broad (*left atrial enlargement*). Signs of *right atrial enlargement* (high and peaked P wave mainly in leads I and II) may also be present

2. *First-degree AV block*

3. *Complete or incomplete RBBB* [Fig 6-22(4)]

It is important to know that as the pulmonary hypertension increases, the following modifications are seen

1. The patterns of leads V_3 to V_4 show an increase in voltage and are "displaced" to the left

2. The patterns of V_1 to V_2 show more typical evidence of RVH; however, the presence of RBBB is revealed by the initial slurring of the R wave (this is interpreted differently by some authors).

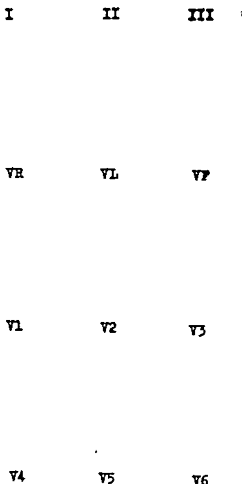


Fig. 6-22(1) Ventricular septal defect. Signs of left ventricular hypertrophy with diastolic overloading. Note large isodiphasic complexes in leads V_3 to V_4

3. The T waves become more negative and of the "ischemic" type in all leads.

In summary, the natural evolution of the electrocardiogram in atrial septal defect[5] is toward a pattern of systolic overload of the right ventricle, which is progressively reached.

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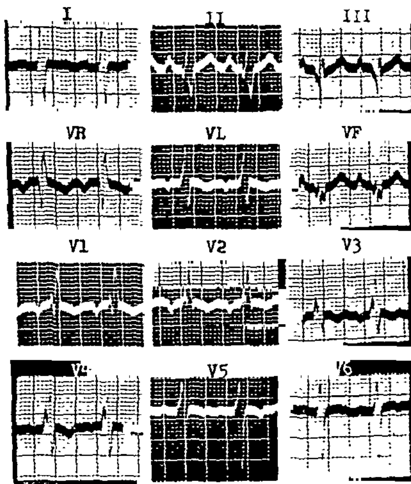


Fig. 6-22(7). Eisenmenger complex Signs of right ventricular hypertrophy in the presence of RBBB. The complexes of Qrs or QrS type in leads III and VF represent the potential variations of the left ventricle. The deep Q wave in these leads is interpreted to indicate hypertrophy of the *left* septal wall, as in ventricular septal defect.

free right ventricular wall) and large isodiphasic complexes in V_3 to V_4 (hypertrophy of the right septal mass).

b. Tall R wave in V_5 to V_6 and in other leads (I and aVL), recording the potential variations of the left ventricle (LVH). The increased forces of the hypertrophied left ventricle account for the tall R wave in lead I and the deep S wave in lead III (left axis deviation).

Ostium Primum. The electrocardiogram in this disease is very similar to that just described for the AV communis (RBBB with AQRS deviated to the left, plus signs of biventricular hypertrophy), with the difference that the RBBB is of a lesser degree

Ebstein's Disease

1 The P wave is of the "congenitale" type or, more characteristically, of the type called "giant"

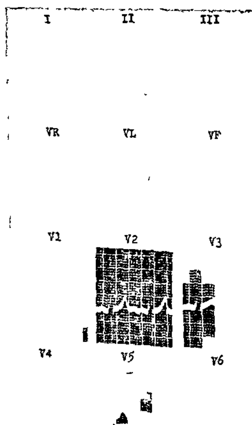


Fig 6-22(3) Patent ductus arteriosus with moderate pulmonary hypertension Signs of biventricular hypertrophy are present, with systolic overloading of the right ventricle and *diastolic* overloading of the left ventricle

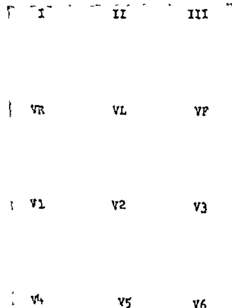


Fig. 6-22(4). Atrial septal defect There is incomplete RBBB The unipolar morphologies belonging to the right ventricle and right septal mass are registered from V_1 through V_4, suggesting right ventricular enlargement.

2 *Atrial arrhythmias* (fibrillation, flutter, paroxysmal tachycardia) are frequently present.

3 First-degree *AV block.*

4. Right bundle branch block with right atrial pattern (qR or qRs) recorded in almost all precordial leads [up to V_5 *in the example* of Fig. 6-22(9)]. These are instances of huge right atrial enlargement (*giant right atrium*). In other cases, the right atrial pattern is recorded in V_1 to V_3, and a left ventricular pattern (qRS with data indicating RBBB) is recorded in the other precordial leads. The tracing would then present only right atrial and left ventricular patterns, with absence of the so-called transitional complex If no RBBB is present, the QR type of complexes with negative T waves (potential variations of the right atrium having normal conduction) may be recorded in several leads, while in the remaining leads the pattern of the left ventricle is observed.

5. *Wolff-Parkinson-White syndrome,* type B [Fig. 6-22(10)]. When observed in a child, this pattern should always suggest the possibility of Ebstein's disease.

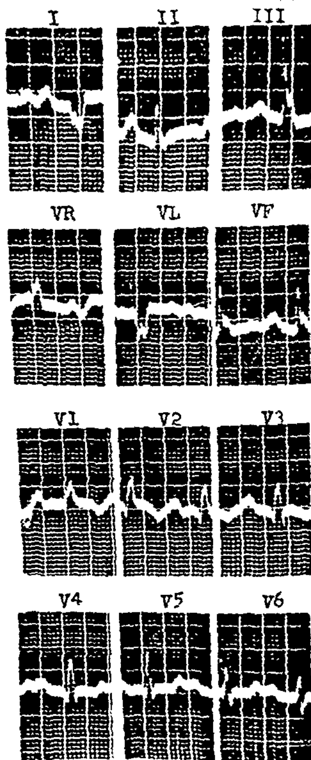


Fig. 6-22(9). Ebstein's disease First-degree AV block and RBBB with the potential variations of the right atrium recorded up to V_5 ("giant" right atrium)

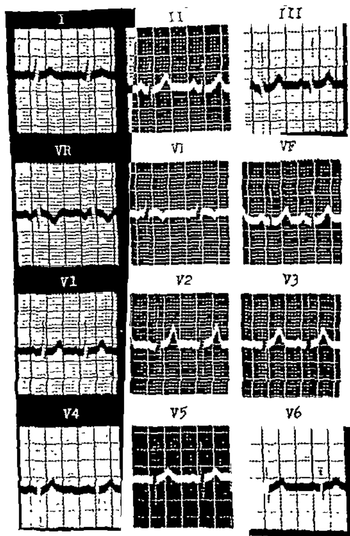


Fig 6-22(6). Pure pulmonary stenosis with right ventricular hypertension (above 100 mm Hg). Signs of right ventricular hypertrophy with systolic overloading in V_1 to V_2 (tall R wave with positive T wave).

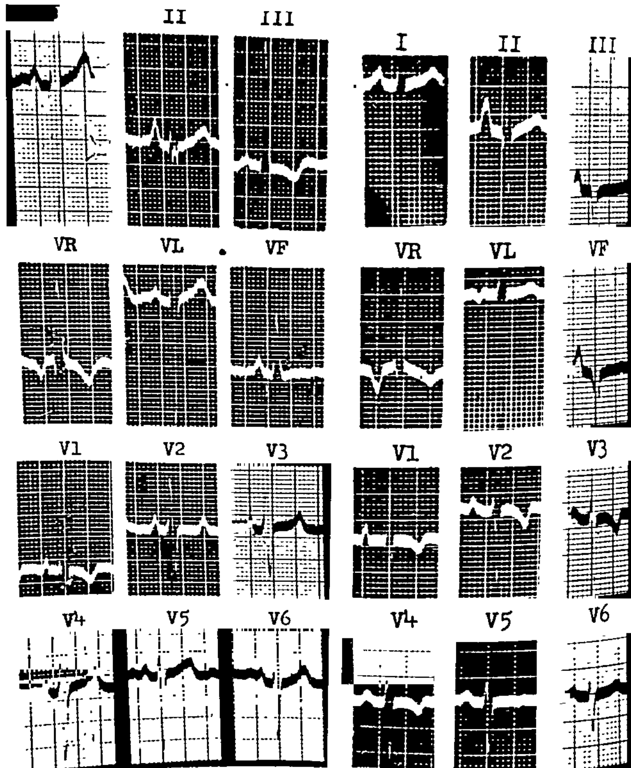


Fig. 6-22(11). Tetralogy of Fallot Signs of right ventricular hypertrophy (free wall and right septal mass).

Fig 6-22(12) Tetralogy of Fallot. Signs of hypertrophy of basal portions of the right ventricle (crista supraventricularis)

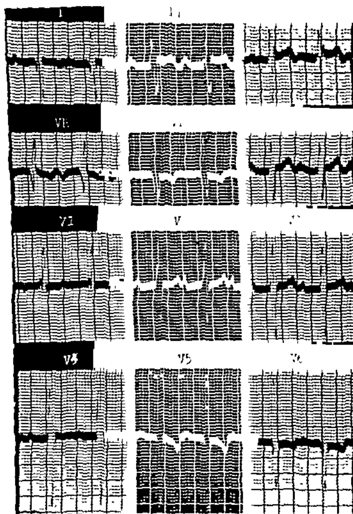


Fig 6-22(8) AV communis Right bundle branch block with left axis deviation and evidence of biventricular hypertrophy.

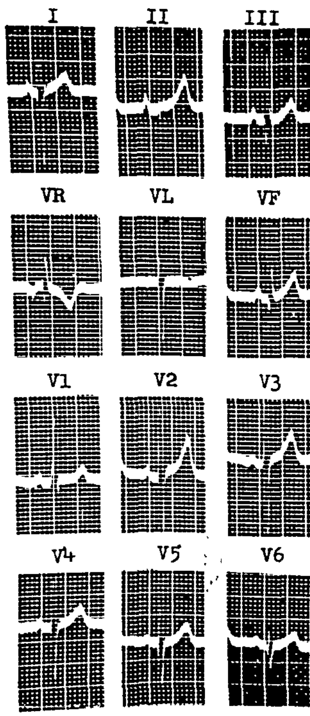


Fig. 6-22(14). Pentalogy of Fallot Signs of biventricular hypertrophy with systolic overloading of the right ventricle and diastolic overloading of the left ventricle.

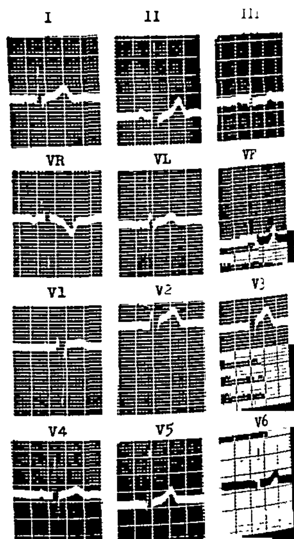


Fig. 6-22(15). Coarctation of the aorta. Signs of left ventricular hypertrophy with no left axis deviation

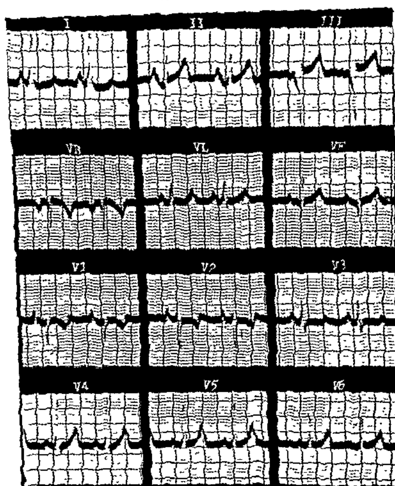


Fig. 6-22(10). Ebstein's disease Wolff-Parkinson-White syndrome, type B.

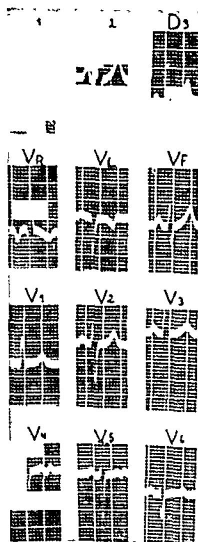


***Fig. 6-22(18)** Transposition of the* great vessels (not corrected) Signs of right ventricular hypertrophy with systolic overloading. Note the T waves of the "infantile type" in V_4 and V_5, and the positive T waves in all other precordial leads

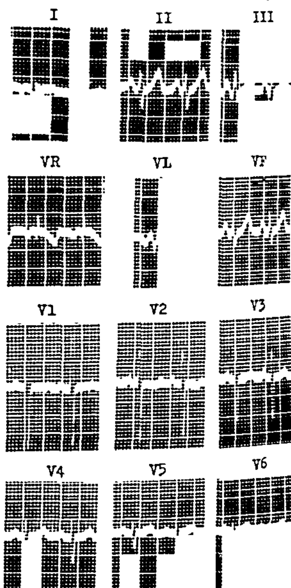


Fig. 6-22(19). "Corrected" transposition of the great vessels Tall, isodiphasic complexes in various precordial leads indicate right ventricular hypertrophy Note the negativity of the P wave in leads I and aVL (transposition of the atria).

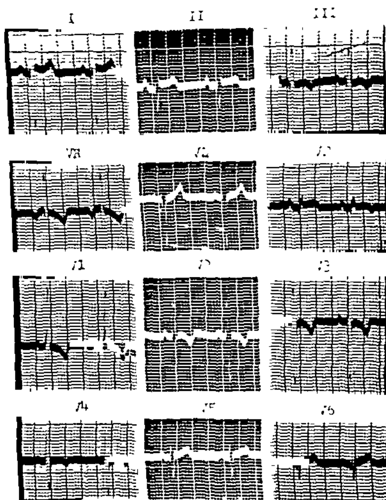


Fig. 6-22(13) Trilogy of Fallot. Signs of "extreme" right ventricular hypertrophy with systolic overloading of the right ventricle.

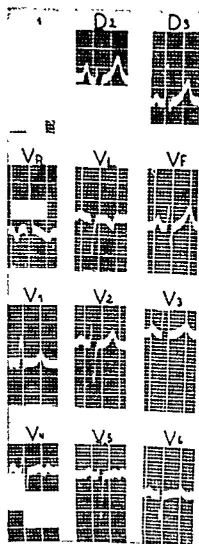


Fig. 6-22(18). Transposition of the great vessels (not corrected). Signs of right ventricular hypertrophy with systolic overloading. Note the T waves of the "infantile type" in V_4 and V_5, and the positive T waves in all other precordial leads.

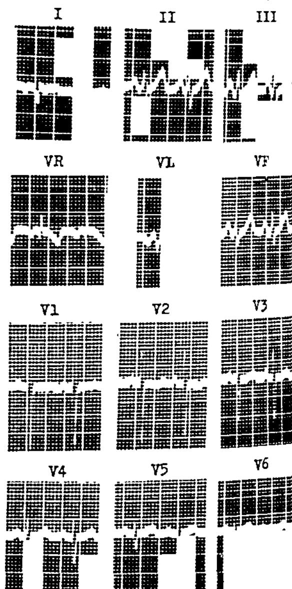


Fig 6-22(19). "Corrected" transposition of the great vessels. Tall, isodiphasic complexes in various precordial leads indicate right ventricular hypertrophy. Note the negativity of the P wave in leads I and aVL (transposition of the atria).

I II III

VR VL VF

V1 V2 V3

V4 V5 V6

Fig 6-22(16). Congenital aortic stenosis. In addition to the electrocardiographic signs of left ventricular hypertrophy, negative T waves of the ischemic type *are present in leads II, III, and aVF (posteroinferior ischemia).*

I II III

VR VL VF

V1 V2 V3

V4 V5 V6

Fig. 6-22(17). Common trunk There are tall R waves in V_1 and V_6 with complexes of the rS type in V_2 and V_3

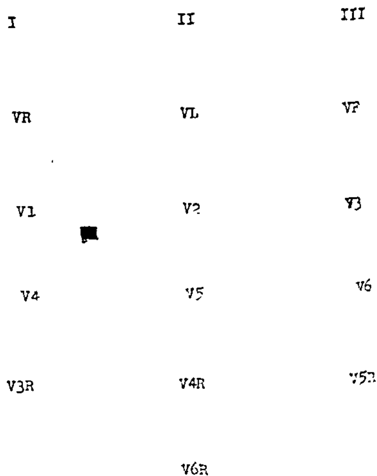


Fig. 6-22(21). Uncomplicated dextrocardia. "Classic" pattern.

Tetralogy of Fallot

1. The P wave is of the congenitale type.

2. There is one of the following indications of RVH

a. Tall R wave in V_1 to V_2 with complexes of the R type with initial slurring, or of the RS or rR types [Fig. 6-22(11)]

b Tall R wave in V_1 followed by rS complexes (potential variations of the trabecular zone of the right ventricle) in the other precordial leads [Fig. 6-22(12)]. In these cases, the hypertrophy of the basal portions of the right ventricle (crista supraventricularis) predominates

3 In marked pulmonary stenosis, the pattern resembles that of the trilogy of Fallot

Trilogy of Fallot

1. The P wave is frequently of the congenitale type, as in the tetralogy of Fallot

2 There is evidence of "extreme" RVH with systolic overload of the right ventricle [tall R wave with negative T wave in V_1 to V_2, and frequently up to V_4, as shown in Fig. 6-22(13)]

3 Elevation of the RS-T segment in leads I and II and less frequently in V_5 to V_6, as pointed out by Medrano

Pentalogy of Fallot. The pattern is similar to that described for tetralogy of Fallot, with RVH [Fig 6-22(11)], it differs in that the signs of associated LVH with diastolic overload are more evident [Fig 6-22(14)].

Coarctation of the Aorta

1. Signs of LVH, which become more manifest with progression of the disease: tall R wave in V_5 to V_6 with delayed intrinsicoid deflection and deep S wave in the right precordial leads [Fig 6-22(15)]

2. ÂQRS is *not* deviated to the left in three-fourths of the cases

Congenital Aortic Stenosis

1 Signs of LVH, as in coarctation of the aorta.

2 *Myocardial ischemia* is frequently present [Fig 6-22(16)]

3 ÂQRS is *not* deviated to the left, as a rule.

Common Trunk

1 Signs of *biventricular hypertrophy* (tall R wave in V_1 to V_2 and in V_5 to V_6) while complexes of the rS type (trabecular zone of the right ventricle) are recorded in V_2 to V_3, as shown in Fig. 6-22(17).

2 The T wave is frequently positive in all precordial leads Patterns of this type need to be differentiated from those of the tetralogy and pentalogy of Fallot.

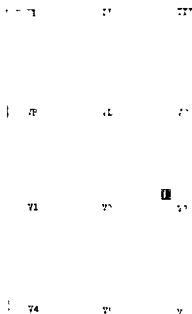


Fig 6-22(20) Single ventricle. Left axis deviation The complexes are essentially negative in all the precordial leads

Transposition of the Great Vessels. NONCORRECTED TRANSPOSITION. This is the common variety of transposition, with the aorta arising from the right ventricle

1. Signs of RVH with systolic overload [Fig 6-22(18)].

2. T waves of the "infantile" type (negative with terminal positivity) have been described in the left precordial leads, accompanied by positive T waves in the right precordial leads (Zuckermann et al.).

CORRECTED TRANSPOSITION. This is the less frequent variety of transposition, in which the ventricles are also transposed, for which reason the transposition of the great vessels becomes "corrected" Electrocardiographically, this variety is difficult to diagnose, the typical patterns of the two ventricles cannot be recognized with certainty on account of the transposition and hypertrophy of the right ventricle. The electrocardiograms in this disease are probably the most difficult to interpret; the presence of . . .

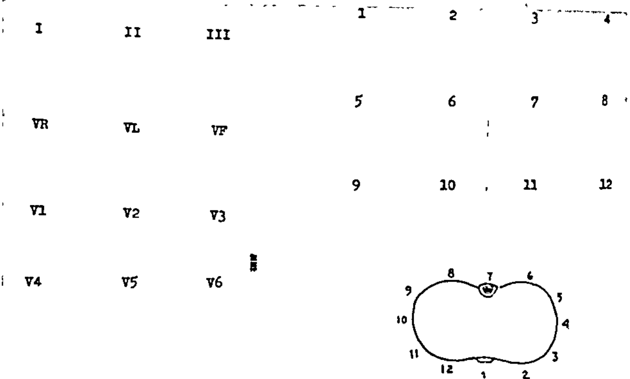


Fig. 6-22(23). Dextrocardia complicated by transposition of the great vessels with the left ventricle on the left side and the right ventricle on the right ("corrected" transposition) 12-lead electrocardiogram (left side of the figure) and thoracic circle (right side). *(Courtesy of the American Heart Journal and of Dr Portillo and coworkers.)*

associated RVH, if such complexes are present, the positive QRS complexes in the other precordial leads are due to the hypertrophied right ventricle, and the negative QRS complexes, to the left ventricle [Fig 6-22(19)]. Negativity of the P wave in lead I speaks for transposition of the atria as well.

Single Ventricle. This malformation may be complicated by other abnormalities (transposition of the great vessels, common trunk, Fallot complexes) which greatly influence the electrocardiogram However, some signs may help: (1) normal P waves, (2) left axis deviation, (3) complexes of the rS or RS type in all precordial leads [Fig 6-22(20)].

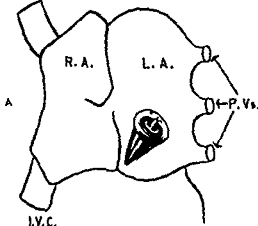
Dextrocardia. UNCOMPLICATED. Under this heading are included the cases of so-called "mirror-image" dextrocardia, with no cardiac abnormality but with situs inversus. In these cases, the electrocardiogram presents a well-known, "classic" pattern [Fig. 6-22(21)].

1 Negative P wave in leads I and aVL[a]
2 "Mirror image" of the QRS complex in the standard and precordial leads

It is important to know that in many cases of uncomplicated dextrocardia, there is *nodal rhythm*. In a normal heart (without dextrocardia), this rhythm is recognized by negative P waves in leads II, III, and aVF and by a positive P wave in aVL, the mean electrical axis of atrial activation (AP) being around −60° [Fig 6-22(22)A]. In nodal rhythm with dextrocardia, the P wave is negative in all limb leads except aVR (where it is maximally positive) since the AP becomes oriented toward −120° [Fig 6-22(22)B]

COMPLICATED Dextrocardia may be complicated by acquired heart diseases, as well as by congenital ones A detailed description of this condition has been made elsewhere (Portillo et al), the position of the various cardiac chambers can occasionally be determined with accuracy through a careful study of the electrocardiogram

The case shown in Fig 6-22(23) is representative The negative P wave in leads I and aVL



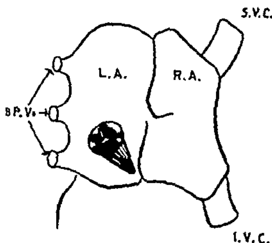


Fig. 6-22(22) The mean electrical axis of P ($\hat{A}P$) in nodal rhythm A Normal heart ($\hat{A}P$ around −60°) B Dextrocardia ($\hat{A}P$ around −120°). *(Courtesy of the American Heart Journal and of Dr Portillo and coworkers.)*

indicates that dextrocardia is present, the recording of a left ventricular pattern (with signs of LVH) from V_2 to V_6, and of right ventricular patterns on the right chest [leads at points 9 to 12 of the thoracic circle represented on the right of Fig. 6-22(23)] indicates that the left ventricle is on the left side and the right ventricle on the right. The post-mortem study revealed dextrocardia with situs inversus, transposition of the great vessels, and left ventricular hypertrophy, the left ventricle was on the left side and the right ventricle was on the right ("corrected" transposition of the great vessels).

[a] It must be remembered that negativity of the P wave in lead I ...
absence of
cardia or c
atrium

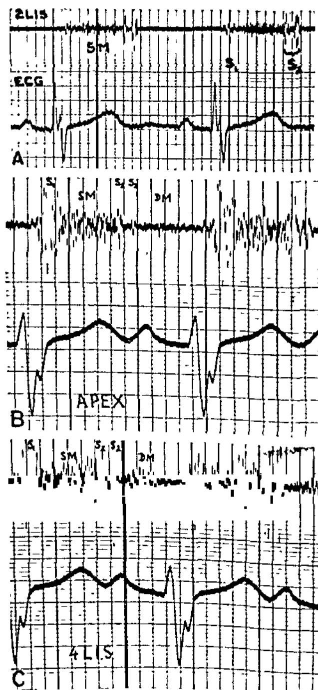


Fig. 6-23. A Phonocardiogram in ostium secundum type atrial septal defect Note the irregular low-intensity ejection-type systolic murmur (SM) and widely split 2d sound (S_2) at the 2d left intercostal space (2 LIS) B Apical murmur of ostium primum type atrial septal defect Note the decrescendo systolic murmur (SM), widely split 2d sound (S_2), and low-frequency mid-diastolic rumble (DM) C. Fourth left intercostal space murmur of same patient with ostium primum type atrial defect Note the plateau or crescendo shape of systolic murmur (SM), split 2d sound (S_2), and middiastolic rumble (DM).

septal defect may best be heard at the lower left sternal border and the apex. It may begin immediately after the 2d sound, or it may have its onset with the 3d sound. Its intensity is usually low, and it is present only in atrial septal defects with a sizable left-to-right shunt and perhaps some cardiac enlargement. The origin of this diastolic rumble is not completely clear, but most likely it is the result of the increased flow across the tricuspid valve.

A high-frequency early *decrescendo diastolic murmur*, characteristic of pulmonary incompetence, may be registered in the relatively rare instances of atrial septal defect associated with pulmonary vascular obstruction.

Atrial Septal Defect—Ostium Primum Type. SOUNDS. The only difference in heart sounds between the primum- and secundum-type defect is that the pulmonary closure in the former may be more accentuated, because of the relatively more frequent association of this defect with pulmonary arterial hypertension.

MURMURS. The *systolic murmur* is of high intensity and is localized to the lower left sternal border and the apex Careful registration suggests that the apical murmur resembles the high-frequency *decrescendo character of mitral regurgitation* and transmits well out to the posterior axillary line (Fig. 6-23B). This is probably the result of a congenital cleft in the mitral valve which is frequently associated with primum-type atrial defect. The lower left sternal border murmur, by contrast, is similar to the *plateau shape* of the murmur caused by the ventricular septal defect and may originate from the high-velocity flow of blood from left ventricle to right atrium or right ventricle during systole (Fig. 6-23C).

Ventricular Septal Defect. SOUNDS. The *1st sound is commonly obscured by the systolic murmur* at the lower left sternal border. The 2d sound is normally split, the aortic and pulmonary elements are seldom more than 0 04 sec apart In cases associated with pulmonary hypertension of some degree, the 2d sound is narrowly split, and the pulmonary element is accentuated An apical 3d sound is noted in most children with sizable left-to-right shunts and cardiac enlargement

MURMURS A very high-intensity, high-frequency *plateau-shaped holosystolic murmur* is registered at the lower left sternal border in

6

Phonocardiography in congenital heart disease

ALEXANDER S. NADAS

INTRODUCTION

The importance of accurate diagnosis in congenital heart disease can scarcely be overstated. Among the tools of diagnosis, the stethoscope has been increasingly emphasized in the past decade. Whereas at first, only the *machinery murmur*, associated with patent ductus arteriosus, was thought to be pathognomonic for a congenital cardiac deformity, in more recent years, the "stenotic" murmurs of semilunar stenosis, the low-frequency apical diastolic murmurs of the large left-to-right lesions, the characteristic auscultatory phenomena of Ebstein's disease, etc., have been recognized as invaluable landmarks for the clinical identification of individual malformations.

The phonocardiograph serves several purposes in this respect. It is an excellent teaching instrument in that it demonstrates visually what *should* be perceived at auscultation. Secondly, by means of various reference tracings, it determines the accurate *timing* of the auscultatory phenomena within the cardiac cycle. Thirdly, by the skillful use of a number of filters, it enables the physician to visualize sound phenomena which lie beyond the reach of the human auditory apparatus. Last, not least, by recording sound phenomena in the same individual through the years, even before and after surgical intervention, an accurate life history of the auscultatory findings may be obtained.

Assuming that the reader is acquainted with the general principles of phonocardiography,[1] it might be well to discuss the auscultatory phenomena of the commonest individual congenital cardiac malformations.

THE LEFT-TO-RIGHT SHUNT GROUP

Atrial Septal Defect—Ostium Secundum Type. SOUNDS. The 1st sound is of average intensity, sometimes wider than normal. The 2d *sound is practically always widely split (more than 0.04 sec)*, the *pulmonary element following the aortic.* The splitting, probably the consequence of the increased stroke volume of the right ventricle, does not vary with respiration, in contrast to the normal, where splitting increases considerably on inspiration. The intensity of both semilunar components is average or is only slightly accentuated. A 3d sound is well registered at the apex in most cases.

MURMURS. The *systolic murmur* of the uncomplicated ostium secundum defect is usually of moderate intensity and rather high frequency and is irregular or diamond-shaped. It begins with the 1st sound and ends usually sometime before the 2d. It is registered best at the 2d left interspace and is present in practically every instance. It is most likely to originate from the right ventricular outflow or the pulmonary artery and probably represents an exaggeration of a physiologic ejection murmur (Fig. 6-23A).

The *low-frequency diastolic murmur* of atrial

[1] See Part 3, Chap. 9. *Editor*

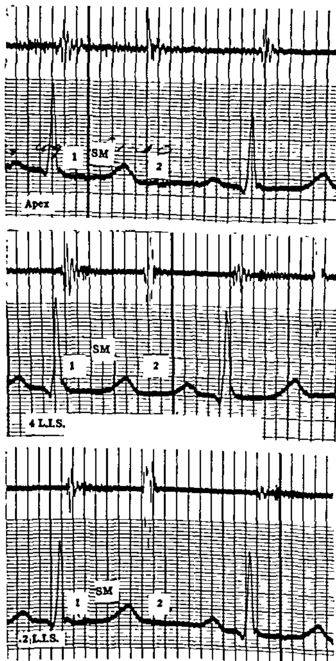


Fig. 6-25. Phonocardiogram of patient with large patent ductus arteriosus and marked pulmonary vascular obstruction with very little shunt. Note the loud 2d sound at the pulmonary area and only faint systolic murmur.

nary artery and the shape of the murmur by the pressure pulse differences between the two large vessels. In patients with a large patent ductus arteriosus, in addition, low-frequency apical middiastolic and systolic murmurs, probably resulting from functional mitral involvement, can be clearly observed.

In patients with patent ductus arteriosus and appreciable pulmonary arterial hypertension, the intensity and the character of the murmur changes. In cases with only moderate diastolic pulmonary hypertension, the diastolic element of the murmur shortens and loses amplitude, in patients with severe pulmonary vascular obstruction and closely identical systolic and diastolic pressure in the aorta and the pulmonary artery, not only may the diastolic element disappear entirely, but also the systolic murmur may become rather insignificant (Fig 6-25). Patients have been seen with a large patent ductus arteriosus and only slight pressure gradient between the two great arteries with *no appreciable murmur at all.* It is worth emphasizing, however, that, in the vast majority of patients with patent ductus arteriosus and pulmonary arterial hypertension, systolic and diastolic—though not necessarily continuous, machinery—murmurs may be observed

Aortopulmonary Fenestration or Rupture of a Sinus of Valsalva. Both these conditions may give rise to auscultatory phenomena indistinguishable from those of a large patent ductus arteriosus. The only two practical auscultatory hints suggesting the presence of one of these conditions (instead of an open ductus) are that (1) the continuous murmur is likely to be maximal in intensity and (2) it is often heard best at the lower rather than the upper left sternal border. The differentiation, however, has to be made in most instances by other clinical and physiologic laboratory methods.

Common Truncus Arteriosus. This rare anomaly, if associated with large pulmonary arteries, may also be hard to distinguish from the auscultatory point of view from a large ductus arteriosus. In view of the anatomic situation, however, the 2d sound is expected to be single, which may represent a subtle point of difference. The continuous murmur—present in about half of the patients with true truncus arteriosus—may be best registered at the 2d left or 2d right interspace, or even over the back (Fig 6-26A). Finally, a harsh lower left sternal border murmur, similar to that described with ventricular septal defect, is almost invariably registered at the lower left or upper right sternal border.

A true truncus arteriosus with hypoplastic pulmonary artery is indistinguishable, not only from the auscultatory, but also from the clinical and physiologic point of view from a severe tetralogy of Fallot.

practically every instance (Fig. 6-24A). This is obviously the result of the systolic ejection of blood from the left ventricle to the right The intensity depends on the size of the orifice and the pressure gradient between the two ventricles. The larger the defect, the more right ventricular hypertension is present, the fainter the murmur.

A low-frequency low-intensity *mid-diastolic* or *presystolic murmur* is noted at the apex in individuals with large left-to-right shunts. A murmur of pulmonary insufficiency is present in cases with severe pulmonary vascular obstruction

Patent D[illegible]

[illegible] less pulmonary arterial hypertension is present as well, in this latter case, of course, the pulmonary element of the 2d sound is definitely accentuated Furthermore, in individuals with the loudest murmur, the 2d sound may be completely enveloped by the characteristic murmur at the 2d left interspace.

MURMURS The typical *machinery murmur* of patent ductus arteriosus begins after an appreciable interval beyond the 1st sound. It consists of high-frequency, high-amplitude uneven vibrations and has a late systolic crescendo, reaching its maximum with the 2d sound (Fig. 6-24B). After the 2d sound, the murmur, without changing frequency, gradually decreases in intensity and trails off *sometime* before the 1st sound of the next cycle. Thus, it can be said that the typical ductus murmur is not only *continuous through both phases of the heart cycle*, but also—and quite importantly—*has no hiatus between the systolic murmur and the 2d sound*. The character and intensity of the ductus *murmur can* probably be explained by the *persistent* systolic and diastolic gradient between the aorta and pulmo-

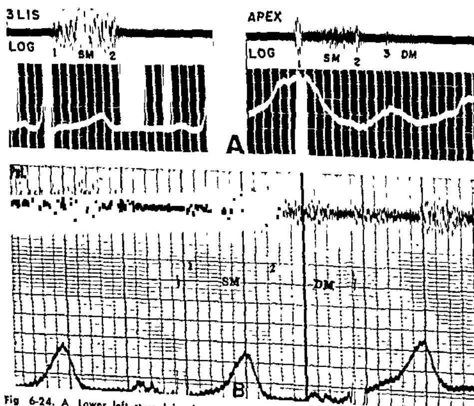


Fig 6-24. A Lower left sternal border and apical sound tracing in patient with ventricular septal defect Reference tracing at apex is apex cardiogram Note high-frequency high-amplitude systolic murmur at 3d left interspace (3 LIS) and 3d sound (S_3) with diastolic murmur at apex B Typical continuous murmur of patent ductus at pulmonary area. Note crescendo systolic and decrescendo diastolic murmur with maximum intensity with the 2d sound

istic, murmur is a *continuous* one, heard over the enlarged intercostal arteries in the back. This, however, is a relatively late phenomenon and is practically never heard under the age of 8 to 10 years

Other frequently observed, but less specific, murmurs are (1) aortic stenosis murmur at the 2d right interspace, (2) aortic regurgitation murmur (due to bicuspid aortic valve?) at the 2d right and 4th left interspace, (3) a lower left sternal border systolic murmur similar to that seen in ventricular septal defect, and (4) an apical low-frequency, low-intensity mid-diastolic murmur

There is no adequate explanation for the last two auscultatory phenomena The middiastolic murmur has been noted in at least 25 per cent of our cases and has been observed with almost equal frequency in patients with a normal-sized heart and those with significant cardiac enlargement

Aortic Stenosis. SOUNDS The 1st heart sound is usually unremarkable. A *late systolic click* (*ejection sound*)—not changing in intensity with respiration—is commonly registered at the 2d right interspace and is probably due to the jet of blood hitting the thin-walled ascending aorta. The aortic closure, in patients with severe stenosis, may be somewhat diminished—but in not nearly so marked a degree as the pulmonary closure diminishes in pulmonary stenosis This is clearly the result of the fact that a sizable and relatively high aortic pressure is necessary for maintenance of life The aortic 2d sound is delayed in patients with severe aortic stenosis—sometimes to the extent that it occurs beyond the pulmonary closure (*paradoxical splitting*). During the height of inspiration, the increased caval flow prolongs right ventricular systole to an extent that pulmonary closure occurs later than normal In normal individuals, whose aortic closure precedes pulmonary closure, this results in a widening in the split of the 2d sound In patients, with severe aortic stenosis, however, whose aortic closure follows pulmonary closure (paradoxical splitting), inspiration causes a narrowing of the distance between the two elements of the 2d sound.

MURMURS The typical systolic murmur of aortic stenosis is *diamond-shaped* and consists of vibrations of high frequency and high amplitude, registered maximally at the 2d right interspace, transmitted well to the neck vessels and the back (Fig. 6-27A). The apex of the diamond, on the whole, is nearer to the 1st sound than in cases with severe pulmonary stenosis. A positive correlation between the severity of the stenosis and the position of the apex of the diamond in systole has been claimed by some authors.[2]

In at least 20 per cent of the patients with congenital aortic stenosis—valvular as well as subvalvular—an early-diastolic blowing murmur may be registered at the 2d right and 4th left interspace.

Congenital Mitral Stenosis and Cor Triatriatum. The auscultatory phenomena may to a greater or lesser degree simulate those of acquired mitral valvular disease.

Pulmonary Stenosis with Intact Ventricular Septum. SOUNDS. The only remarkable thing about the 1st sound in this condition is that it is commonly followed, particularly on expiration, by *an ejection sound*—a *systolic click*—at the pulmonary area. Frequently, though not invariably, this denotes mild stenosis, almost without exception it occurs with valvular stenosis and poststenotic dilatation.

The characteristics of the 2d sound in pulmonary stenosis with intact ventricular septum have been discussed extensively. As has been pointed out before,[3] under normal circumstances—because of the nature of the pressure pulses—pulmonary closure follows aortic closure by 0.02 to 0.04 sec As a rule, in healthy subjects, pulmonary closure is registered with higher amplitude at the 2d left interspace, then aortic closure. In pulmonary stenosis with intact ventricular septum depending upon the severity of the stenosis—both the distance between aortic and pulmonary elements and the intensity of pulmonary closure itself may undergo significant changes The more severe the pulmonary outflow obstruction, the longer the right ventricular systole, the wider the splitting of the 2d sound. Also, the lower the pulmonary arterial pressure, the fainter the result of pulmonary closure, till in individuals with maximal stenosis it cannot be heard or even registered at all

A *4th sound* (or presystolic gallop) associated with right atrial hypertension is clearly

[2] See Part 7, Chap. 9. *Editor*

[3] See Part 2, Chap. 10 and Part 3, Chap. 9, Clinical Phonocardiography. *Editor.*

VALVULAR AND VASCULAR LESIONS WITH A RIGHT-TO-LEFT SHUNT OR NO SHUNT

Coarctation of the Aorta. SOUNDS The 2d sound is usually loudest in the aortic area; of the two elements, the aortic is loudest. The presence of an apical 3d sound is not unusual, particularly in children.

MURMURS. The most characteristic—almost pathognomonic—auscultatory phenomenon of coarctation of the aorta is a *high-frequency, moderately high-amplitude diamond-shaped murmur,* maximally heard over either side of the spine. This is presumably caused by the coarcted segment of the aorta itself (Fig 6-26B).

The second, and almost equally character-

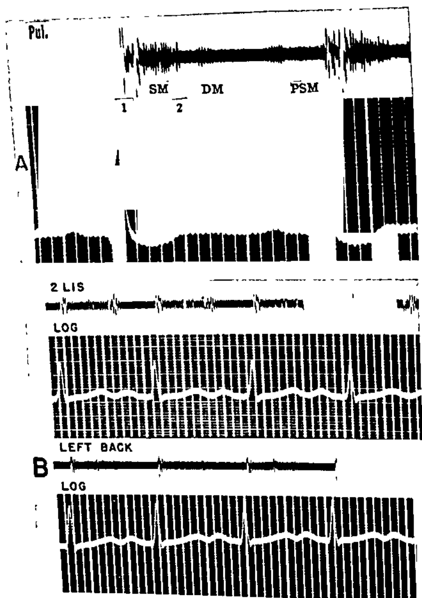


Fig 6-26 A. Phonocardiogram of patient with common truncus arteriosus. Note 1st sound and systolic click, decrescendo systolic murmur, and mid-diastolic presystolic (DM, PSM) rumble. B Sound tracings in patient with coarctation of the aorta. Note continuous murmur at 2d left interspace and back. The systolic murmur at 2d left interspace (2 LIS) is suggestively diamond-shaped.

registered in patients with severe pulmonary stenosis.

MURMURS. The systolic murmur of pure pulmonary stenosis is *diamond-shaped* and is best registered at the pulmonic area. The vibrations are of high frequency and usually of high intensity. The murmur transmits very well to the neck and the back A rather good correlation exists between the severity of the stenosis and the position of the apex of the diamond in systole. The *later the peak of the diamond,* the *more severe the stenosis* (Fig. 6-27B). Almost invariably, in patients with severe pure pulmonary stenosis, the apex of the diamond is beyond the first half systole. Since pulmonary closure is late, blood continues to flow through the pulmonary valve beyond aortic closure, pulmonary closure is faint, *thus, the impression of an early diastolic murmur may be created by the prolonged pulmonary systolic murmur extending beyond the well-registered aortic closure.*

In rare instances of maximal pure pulmonary stenosis, accompanying tricuspid valve abnormalities may result in murmurs of tricuspid regurgitation and tricuspid stenosis.

The Tetralogy of Fallot. SOUNDS. The 1st sound is loudest at the lower left sternal border. Usually, it is not split. The *2d sound is almost invariably single and loud at the lower left sternal border.* It probably represents aortic closure exclusively, with very little pulmonary element added to it. Only a very diminished 2d sound is heard at the pulmonary area—this probably corresponds also to aortic closure. The *closure of the pulmonary valve is so faint and probably so close to aortic closure that it is almost never audible and seldom demonstrable by phonocardiography.*

MURMURS. The characteristic murmur of the

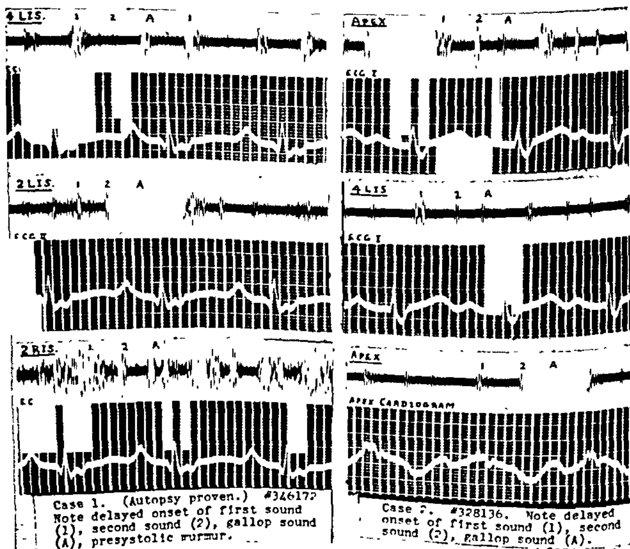


Fig. 6-28. Phonocardiogram of two patients with Ebstein's anomaly.

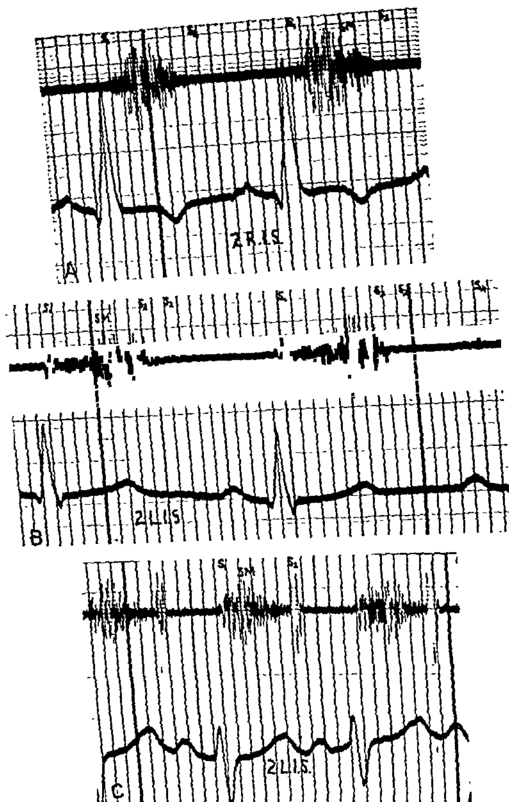


Fig. 6-27. A Phonocardiogram at 2d right interspa[illegible] the early diamond-shaped systolic murmur [illegible] 2d left interspace in patient with pure pu[illegible] systolic murmur and widely split 2d sound. C [illegible]ogram at 2d left interspace of patient with pulmonary stenosis and ventricular septal defect (tetralogy of Fallot). The apex of the diamond-shaped murmur is close to the 1st sound, and the 2d sound is not split.

7

Electrokymography in congenital heart disease

GIANO MAGRI

In contrast with the number of studies of electrokymography published since 1946, only few contributions have appeared dealing with congenital heart disease. This might be related to the difficulties of the method and the necessity of good collaboration of the patient, which renders its application to infants more difficult. In spite of this, several observations have appeared since 1950, including the outstanding work of Kjellberg et al In addition, special publications have been devoted to electrokymography in congenital heart diseases (Donzelot et al., Luisada and Fleischner, 1949; Magistretti et al., 1956, Magri et al, 1957).

Data of some interest may be obtained from the study of either the border tracings of the cardiovascular silhouette (right atrium, right ventricle, [illegible]

the deflections recorded. Therefore, the same degree of amplification should be used for the various structures It is obvious that, when one mentions a decrease of amplitude of pulsations from the hila to the periphery of the lungs, the comparison is made between tracings recorded with the same amplification. One can either study the general patterns of the tracings or measure the basic phases of the cardiac cycle. For the study of patterns, a film speed of 50 mm/sec is sufficient, while for accurate measurements, film speeds of 75 to 100 mm/sec or more are necessary. As many patients with congenital heart disease are submitted to catheterization, in some cases a simultaneous record of intracardiac pressure curves and of the ECG with the EKy allows a more exact interpretation of the electrokymographic waves.

In spite of the great variety of congenital malformations, some degree of schematization of the EKy changes is possible. Characteristic patterns have been observed in cases with increased or decreased pulmonary flow, in pulmonary hypertension, and in pulmonic or aortic stenosis In more complex malformations, the modifications of the EKy may be similar to those observed in certain basic hemodynamic syndromes and contribute little to an exact anatomic diagnosis of the disease. For this reason, the following description, far from complete, will be limited to some of the most common malformations for which sufficient data have been collected.

Pulmonic Stenosis. The most interesting tracings are obtained over the pulmonary artery. In general, the pulsations of the artery are *decreased*, but in valvular stenosis, they might be increased over the initial part. For this reason, the valvular and the infundibular stenosis should be considered separately.

VALVULAR STENOSIS. The degree of stenosis is important in causing the electrokymographic changes According to Kjellberg and coworkers, in cases of moderate stenosis with a pressure gradient of less than 30 mm Hg, the incisura and the dicrotic wave appear poorly defined. When the gradient is more than 30 mm Hg, an *anacrotic notch* appears over the

tetralogy of Fallot syndrome is a *stenotic pulmonary ejection murmur* (Fig 6-27C) It is different in some characteristic ways from that audible in pure pulmonary stenosis (1) the murmur of the tetralogy of Fallot is loudest at the mid- and lower left sternal border, rather than the upper left sternal border, probably because of the infundibular nature of the obstruction; (2) the right and left ventricular pressure pulses in this condition are so similar to each other that the peak ejection of the blood through the pulmonary outflow tract occurs relatively early, as a consequence, the apex of the diamond-shaped murmur occurs usually early, that is, within the first half of systole, (3) the transmission of the Fallot murmur is not so wide, particularly to the neck, as the stenotic murmur of pure pulmonary stenosis

One may state with fair assurance that the *intensity of the murmur in the tetralogy of Fallot is in inverse proportion to the severity of the disease* As a matter of fact, a child who, when feeling well, has a loud rasping systolic murmur may have no murmur at all during a hypercyanotic spell This is probably the result of markedly diminished flow of blood through the pulmonary outflow tract Some of the most severe cases of tetralogy of Fallot, those with functional or anatomic pulmonary atresia, may have no murmurs at all

It is interesting to note that, although in patients with a ventricular defect and left-to-right shunt typical murmurs attributable to the septal defect are heard, in situations where the shunt across the ventricular defect is exclusively in the right-to-left direction, no murmurs are audible It should also be mentioned that older children and adults with maximal pulmonary obstruction usually have continuous "collateral" murmurs over the back and under the clavicle.

Tricuspid Atresia. The auscultatory phenomena are indistinguishable—on the basis of present information—from those observed in patients with tetralogy of Fallot.

Ebstein's Anomaly Patients with downward displacement of the tricuspid valve have rather characteristic auscultatory findings.

SOUNDS. A *triple* or *quadruple rhythm* is registered almost without exception The components of this are (1) late 1st sound, (2) well-split and low-intensity 2d sound, (3) atrial sound and occasional 3d sound The 2d sound at the pulmonary area is diminished in intensity.

MURMURS Most of the murmurs in Ebstein's anomaly originate at the tricuspid valve. A scratchy, regurgitant murmur increasing with inspiration at the lower left sternal border and an atrial systolic (presystolic) murmur at the apex are typical auscultatory phenomena (Fig 6-28).

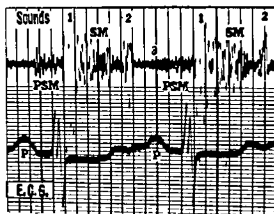


Fig 6-29. Phonocardiogram at apex of patient with complete transposition of pulmonary veins Note the triple rhythm and systolic and presystolic murmur.

THE TRANSPOSITIONS

Transposition of the Pulmonary Veins. Partial transposition is indistinguishable from the auscultatory viewpoint from a secundum-type atrial septal defect. The phonocardiographic picture of a complete transposition of the pulmonary veins in many ways is similar to Ebstein's disease. Triple or quadruple rhythms are common, and murmurs of tricuspid regurgitation and stenosis are present in the typical cases (Fig 6-29).

Transposition of the Great Arteries. SOUNDS. The 2d sound in the pulmonary area is usually diminished. At the lower left sternal border, loud and single 1st and 2d sounds are registered.

MURMURS. About a third of the patients have no murmurs. The others show a lower left sternal border systolic murmur which may have the characteristics of a ventricular defect or an infundibular stenosis. Very occasionally, an apical low-frequency diastolic murmur is also demonstrable.

increased ventricular dynamics are in contrast with the dynamics of the pulmonary artery.

OTHER TRACINGS. The aortic pulses and the left ventricular curve pulses are often normal, but in some cases, a reduced amplitude of the ventricular motions can be observed. This seems due to a decreased venous return to the left heart.

Trilogy of Fallot. When pulmonary stenosis is associated with an interventricular septal defect, unimportant variations are observed over the pulmonary artery and the right cardiac cavities. If, in addition, there is also an atrial right-to-left shunt, the EKy of the left atrium is modified and may even assume the pattern of mitral insufficiency.

Tetralogy of Fallot. The particular structural malformation may render it difficult to obtain records of the pulses of the pulmonary artery. If recorded, the pulmonic pattern is typical of infundibular stenosis. In one case, reported by Kjellberg and coworkers, a negative pulsation was recorded over the infundibulum. The *pulsations of the peripheral pulmonary fields are generally decreased and may be absent.* However, in two personal cases, *good pulsations of atrial type have been observed over the lungs.* This pattern is probably due to the pulsations of the pulmonary veins. The right ventricular and right atrial curves show the overload and strain of these chambers. An increase of the atrial waves and a delay of ventricular ejection have been noted. Good pulsations have been recorded over the left ventricle and aorta (Fig. 6-31).

In *pentalogy of Fallot,* the additional atrial septal defect may cause large left atrial waves, as in the trilogy of Fallot.

Pulmonary Hypertension. In pulmonary hypertension, the *pulmonary arterial pulse* has the following typical pattern: (1) delay of the foot of the wave (measured from the Q of the ECG); (2) slower rise; (3) marked delay of the peak of the wave, which falls in late systole; (4) decreased amplitude and early dicrotic wave. The *right atrial tracing* may show evidence of powerful atrial contractions. Both this and the evidence of delayed right ventricular ejection have been observed in all cases in which the flow from the right chambers was opposed (pulmonary stenosis, constrictive pericarditis); therefore, these patterns are not specific. In some cases, *wide pulsations are recorded over the pulmonary trunk, in contrast with the small pulsations of the peripheral pulmonary fields* (Luisada and Fleischner). This difference is especially evident in cases of thrombosis of the small arterial vessels In such

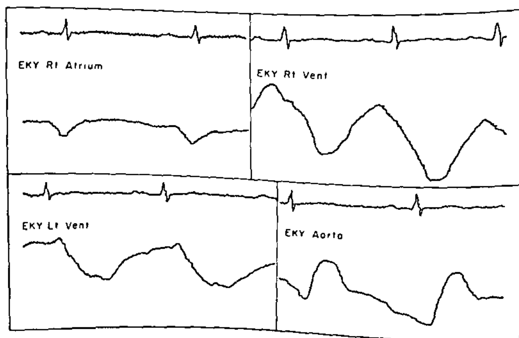


Fig 6-31. Tetralogy of Fallot in an 18-year-old boy The EKy of the right atrium, recorded in the P-A position, shows a deep presystolic wave. The EKy of the right ventricle (in LAO) shows a high positive presystolic wave, synchronous with the atrial contraction. The aortic pulse is within normal limits. It was not possible to record the pulsations of the pulmonary artery.

ascending branch of the pulse: *the higher the* pressure gradient, the lower is this notch In addition, *there may be a rounding of the peak* of the wave and the presence of some *vibrations*, revealing the turbulence of flow. In moderate stenosis (gradient RV-PA around 80 mm Hg), the anacrotic notch is deeper and lower while the peak is sharper (Fig. 6-30A). *In severe* stenosis (gradient RV-PA around 125 mm Hg *or more*), the changes are even more evident: the incisura and the dicrotic wave are delayed, are smaller, and may disappear, while the anacrotic notch is not always visible (Fig 6-30B). The most common aspect of the pulse of the pulmonary artery is a *typical anacrotic pulse with rounded and delayed apex*; sometimes it is *plateau-like* and may be concave, according to Donzelot and coworkers. The markedly reduced amplitude of pulsations of the peripheral pulmonary fields often corresponds to an increase of pulsations of the pulmonary trunk, which is due to the poststenotic eddies which dilate the main artery

INFUNDIBULAR STENOSIS The pulmonary trunk has no increase of pulsations. In 9 out of 11 cases studied by Kjellberg and coworkers, small pulse waves were found on the pulmonary artery. The pattern was such that it was difficult to distinguish any peak of the waves. In addition, both the incisura and the dicrotic *notch* were delayed. While cases with valvular stenosis may present pulses with an anacrotic notch in the ascending limb, *cases with infundibular stenosis never show this detail.* Cases with postvalvular stenosis present pulses similar to those observed in valvular stenosis. It should be emphasized that an anacrotic notch can be observed in other heart diseases, such as mitral stenosis and cor pulmonale. However, in these conditions, both the incisura and the dicrotic notch are wide and are not delayed. In these cases, the slit of the electrokymograph should not be placed too low, in order not to record the motions of the left atrium (Kjellberg et al.). Study of the pulmonary artery gives important data, but is not possible in many cases because *the pulses are too small and even imperceptible.* On the other hand, tracings recorded over other segments of the cardiovascular silhouette may show characteristic patterns.

RIGHT VENTRICLE. A prolonged ejection period (over 0.30 sec) and a short isometric period have been *described* It is necessary to remember that, in the PA position, it is often difficult to record the right ventricular tracing, the curve looks like that of the atrial EKy. On the contrary, a good tracing can be obtained in the LAO position

RIGHT ATRIUM. Various authors agree about the abnormal amplitude of the presystolic wave, indicating strong right atrial contraction. The increased atrial and ventricular pulsations which can be recorded over the lower right arch are in contrast with the decreased *pulsations* of the pulmonic arch. In other words, the

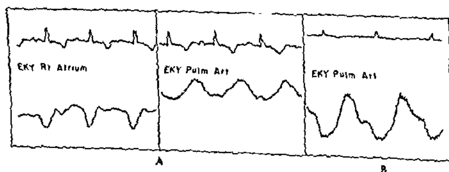


Fig. 6-30. The EKy tracings in two cases of pulmonic *stenosis. A, Patient* age 18 years with valvular stenosis (right *ventricle, 120; pulmonary artery, 15 with a* gradient of 105 mm Hg). The EKy of the right *atrium shows a* deep, negative presystolic wave. *The EKy* of the pulmonary artery shows a slow rise of the *pulse and on early* anacrotic notch. The peak of the pulse is sharp and is recorded 0.26 sec *from the* beginning of the wave (0.38 sec from Q). B. *Patient* age 24 years with *valvular stenosis (very high* pressure *gradient.* right ventricle, 150; pulmonary artery, 10 mm Hg). *The EKy,* recorded over the origin of the *pulmonary* artery, shows good pulsations The pulse rises slowly at first, then more rapidly. The peak is *delayed* (0.34 sec from Q). *The incisura and dicrotic wave are visible, but severely* delayed.

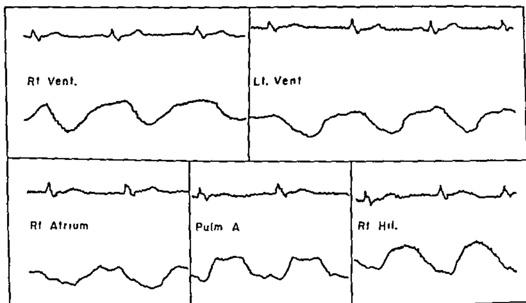


Fig. 6-33. Ventricular septal defect in a 36-year-old man. The ventricular tracings are within normal limits. The EKy of the right atrium shows a positive presystolic wave. There is a plateau-like pattern over the pulmonary artery, unusual in this anomaly, and there are increased hilar pulsations.

seen by the author· 140/20 mm Hg). In the typical cases having pulmonary hypertension and a severely dilated pulmonary artery, the ascending branch of the pulmonic pulse is prolonged, the peak of the wave is rounded, and the descending branch is also prolonged (Figs. 6-34 and 6-35).

Truncus Arteriosus. In a case observed by Kjellberg and coworkers, the pulmonary pulse had the same pattern as that observed in pulmonary hypertension; the aortic pulse had a delayed incisura and a late dicrotic wave, because of the increased flow and the greater pulse pressure. According to Donzelot and coworkers (four cases), the pulmonary pulses are low and indistinct. However, there are not sufficient data for an exact description of the EKy pattern in this malformation.

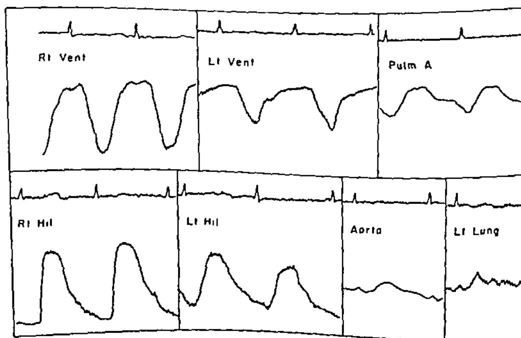


Fig. 6-34. Eisenmenger's complex plus tricuspid insufficiency in a 19-year-old boy Large pulsations of the right ventricular border (LAO position). The pulse of the pulmonary artery shows a slow rise and a rounded peak. The dicrotic wave is small and delayed. There are good pulsations of the hila and small pulsations of the peripheral pulmonary fields

ascending branch of the pulse: the higher the pressure gradient, the lower is this notch. In addition, there may be a *rounding of the peak* of the wave and the presence of some *vibrations*, revealing the turbulence of flow. In moderate stenosis (gradient RV-PA around 80 mm Hg), the anacrotic notch is deeper and lower while the peak is sharper (Fig. 6-30A). In severe stenosis (gradient RV-PA around 125 mm Hg or more), the changes are even more evident. the incisura and the dicrotic wave are delayed, are smaller, and may disappear, while the anacrotic notch is not always visible (Fig 6-30B). The most common aspect of the pulse of the pulmonary artery is a *typical anacrotic pulse with rounded and delayed apex;* sometimes it is *plateau-like* and may be *concave*, according to Donzelot and coworkers The markedly reduced amplitude of pulsations of the peripheral pulmonary fields often corresponds to an increase of pulsations of the pulmonary trunk, which is due to the poststenotic eddies which dilate the main artery.

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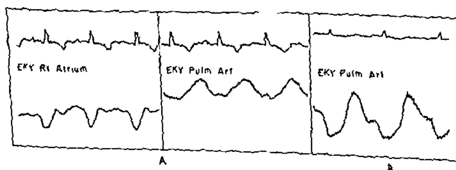


Fig 6-30 The EKy tracings in two cases of *pulmonic stenosis* A Patient age 18 years with valvular stenosis (right ventricle, 120; pulmonary artery, 15 with a gradient of 105 mm Hg). The EKy of the right atrium shows a deep, negative presystolic wave The EKy of the pulmonary artery shows a slow rise of the *pulse and an early anacrotic notch* The peak of the pulse is sharp and is recorded 0.26 sec from the *beginning* of the wave (0.38 sec from Q). B. Patient age 24 years with valvular stenosis (very *high pressure* gradient right ventricle, 150; pulmonary artery, 10 mm Hg) The EKy, *recorded over* the origin of the pulmonary artery, shows good pulsations The pulse rises slowly at first, then more rapidly. The peak is delayed (0.34 sec from Q). The incisura and dicrotic wave are visible, but severely delayed.

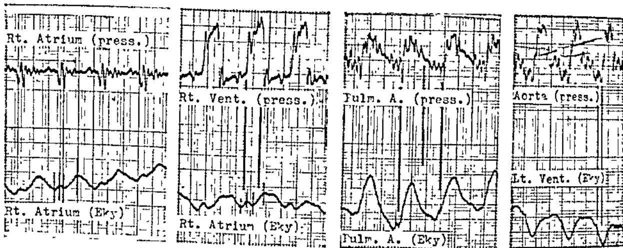


Fig. 6-37. Patent ductus arteriosus in a 32-year-old woman. Simultaneous EKy and pressure tracing. Normal atrial waves and rapid pulmonic pulse (speed, 25 mm/sec).

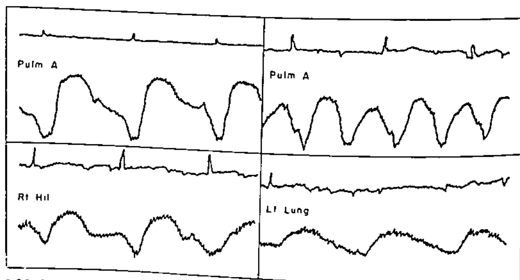


Fig. 6-38. Patent ductus arteriosus in a 20-year-old woman. EKy recorded over pulmonary artery, hili and peripheral pulmonary fields Large pulmonary pulse, rounded peak, high dicrotic waves In some segments of the vessel, a double impulse is recorded Normal speed of the pulmonic pulse wave toward the periphery of the lungs Pressures· aorta, 130/50; pulmonary artery, 130/65; right ventricle, 130/0.

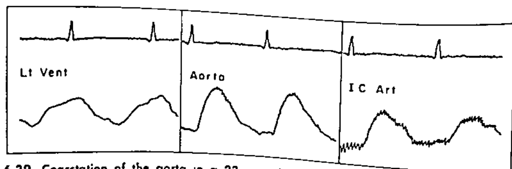


Fig. 6-39. Coarctation of the aorta in a 22-year-old man Normal pattern of the aortic pulse Marked pulsations of the intercostal arteries

cases, strong right ventricular pulsations and *small left ventricular pulsations* are recorded, on account of decreased venous return to the left heart with a decreased left ventricular output.

Atrial Septal Defect. The tracings recorded over the lower right border or the pulmonary conus and the densograms of the hilar shadows or the periphery of the lungs are similar in this defect and in anomalous venous drainage. The fundamental picture is that of an increased pulmonary flow. The pulse of the pulmonary artery has a typical appearance, the foot of the wave is not delayed, the peak of the wave falls early (pulsus celer). This pattern is related to the increased volume of ejection and to the speed of the wave ejected from the right ventricle without increase of peripheral resistances. This, however, is not true in all the cases, especially in adults, because changes of the pulmonary vessels may cause an increase of peripheral resistance For this reason, *the peak of the wave may be rounded and delayed*, indicating this secondary abnormality (Fig. 6-32). The dicrotic wave is wide and falls in the second half of the descending branch of the pulse The pulsations of the hilar shadows are increased, and the peripheral pulmonary fields also have large pulsations. The interval between central and peripheral pulmonary pulses is decreased (high speed and normal peripheral resistances).

RIGHT VENTRICLE. According to Magistretti et al, diastole of the right ventricle is completed after that of the left. Isometric contraction, on the contrary, is slightly shorter than on the left side, and so is isometric relaxation.

RIGHT ATRIUM In two cases seen by the author, the presystolic atrial waves were large (Fig. 6-32). An additional positive systolic wave related to the shunt has been described but is far from being constant.

LEFT HEART An increase of the pulsations of the right and a reduction of the pulsations of the left cardiac contour have been considered typical. This fact is only relative, therefore, it is possible to observe "normal" pulsations on the left side. No morphologic alterations of the waves have been observed.

Ventricular Septal Defect. According to the majority of authors, the tracings are within normal limits. However, Luisada and Fleischner described an increased amplitude of the pulmonary artery pulsations and a pulsus celer over the hila and the peripheral pulmonary fields, without increase of the speed of the pulse. Kjellberg and coworkers, in 13 out of 25 cases, observed a slower rise and a longer duration of the pulmonary pulse (0 15 to 0.20 sec), the peak was in late systole, the incisura was premature, and the diastolic wave was small. The tracings, therefore, are similar to those of the pulmonary hypertension. The most important data consist of an increased amplitude of the pulmonary pulsations extending to the hila and the periphery of the lungs. Both ventricular borders present large pulsations. The right atrial curve has good waves, and the presystolic waves are very evident (Fig. 6-33). The aortic pulsations are normal.

Eisenmenger's Complex. The pulsations are increased over both the right and the left ventricular contours and also over the pulmonary trunk. Large pulsations are observed over the hila. Reduced pulsations have been observed over the peripheral pulmonary fields (Fig. 6-34), at least in cases with very high pressure in the pulmonary artery (in a case

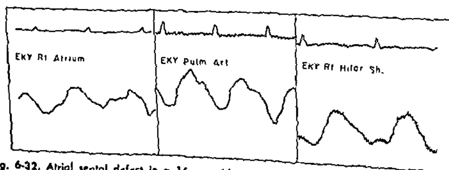


Fig. 6-32. Atrial septal defect in a 16-year-old girl. The EKy of the right atrium shows large positive systolic waves The pulmonary pulse is rounded, and the peak is delayed (0.30 sec after Q). Good pulsations are observed over the hilar region.

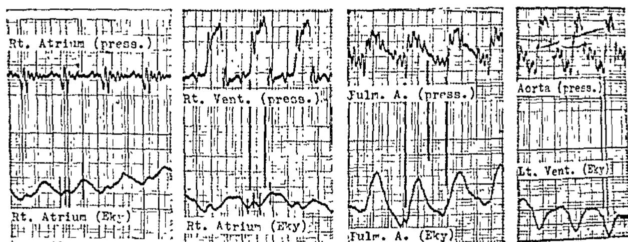


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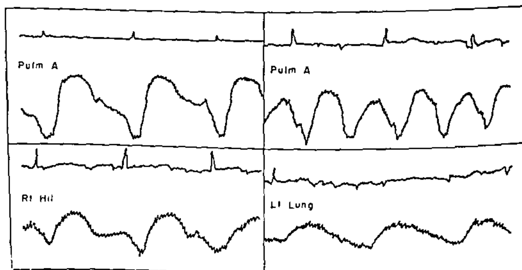


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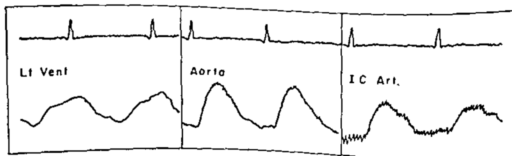


Fig. 6-39. Coarctation of the aorta in a 22-year-old man Normal pattern of the aortic pulse. Marked pulsations of the intercostal arteries

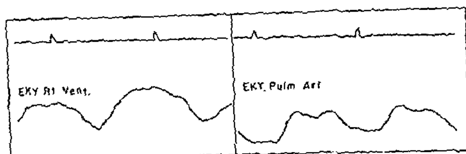


Fig. 6-35. Eisenmenger's complex plus anomalous venous return in a 19-year-old boy. Right ventricle pressure, 140/5, pulmonary artery pressure, 120/60. There are severe changes of the pulmonary pulses and a high dicrotic wave.

Patent Ductus Arteriosus. The EKys recorded over the large vessels give the best information

AORTIC PULSE. This is large and almost similar to that recorded in aortic insufficiency. However, the pulse is more rounded than in aortic insufficiency (Figs 6-36 to 6-38) The foot of the wave may occur early, while both the incisura and the dicrotic wave are accentuated. However, in many cases, the tracing is within normal limits. If there is a reversed shunt, *the aortic tracing is abnormal* In such a case, the foot of the curve is delayed and the peak is pointed. The incisura is more evident, *and the dicrotic wave is increased.*

PULMONIC PULSE. The pulse often has a typical pattern there are large pulsations with a rapid rise (Figs. 6-36 to 6-38). The pulse may be similar to that recorded in pulmonary hypertension. The peak may be followed by a plateau and a typical notch. According to *Donzelot and coworkers*, an anacrotic notch would be due to the shunt. The dicrotic wave is described as displaced toward the peak of the pulse A *peaked diastolic wave on the descending branch of the pulse wave has also been described* (Fig 6-38). These typical patterns have been observed by several authors *and are probably due to the shunt. In two out of three cases, this wave was observed also* over the pulmonic fields. It should be emphasized that this wave was not observed in a case in which the pulmonary pulse was delayed and rounded, and in which cardiac catheterization showed a high diastolic pulmonary *pressure*

PERIPHERAL PULMONARY FIELDS The arterial pulsations are high and rapid and show a well-marked *dicrotic wave* An increase of the speed of the pulse waves has been observed (Luisada and Fleischner).

LEFT ATRIUM. Because of the increased flow, larger atrial contractions are recorded. On the contrary, the ventricular tracing is usually normal

Aortic Stenosis. The tracing of the aortic arch, the left ventricular tracing, and the left atrial tracing present *interesting data*

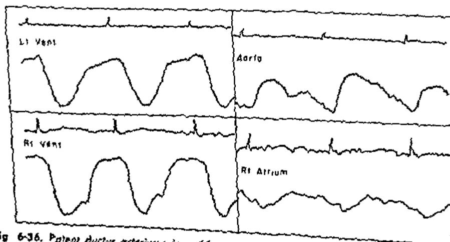


Fig 6-36. *Patent ductus arteriosus in a 16-year-old girl. Large ventricular pulsations; rounded aortic pulses with high dicrotic wave (right ventricle pressure, 25; pulmonary artery pressure, 20).*

Blood in congenital heart disease

MARIO STEFANINI AND FRANCO GOBBI

There are significant changes in morphologic and chemical constituents of the blood in the course of some congenital heart diseases. A review of the literature indicates that this subject has been discussed often but has seldom received adequate treatment.

A few generalizations may be made as introductory remarks *Significant blood changes are found in congenital heart disease only when venous-arterial shunts or other anomalies, important enough to induce cyanosis, are present.* Two findings are outstanding (1) *increased red cell mass* with relative lack of involvement of the other formed elements of the blood, this produces the classic picture of secondary polycythemia, (2) defects in the hemostatic and blood-clotting mechanisms leading to *blood hypocoagulability* and, under certain circumstances, to severe bleeding All changes revert to normal after successful corrective surgery They will be discussed separately.

SECONDARY POLYCYTHEMIA

The polycythemic state of cyanotic congenital heart disease is a compensatory mechanism to the low arterial blood O_2 saturation and tissue hypoxia. Thus, it is constantly associated with cyanosis and clubbing of the fingers (Fig 6-40) severe dyspnea, etc. The liver and spleen may be palpable in a small number of cases (Lawrence).

Blood findings are those typical of polycythemia of the so-called secondary type (Table 6-3) Erythrocyte count, hemoglobin level, and hematocrit are very high. White cell and neutrophil counts may be slightly above normal but are most often normal; platelets are never above the normal range and are, in fact, dras-



Fig. 6-40. Congenital heart disease with cyanosis (Eisenmenger's syndrome). Note clubbing of the fingers and toes. Hematologic and other findings are described in Table 6-3.

AORTIC PULSE. The foot of the wave generally is normal, while the ascending branch is prolonged; it is possible to observe an anacrotic notch, but this is less frequent than in pulmonic stenosis. The peak of the wave, generally rounded, is delayed. The incisura and the dicrotic wave are less evident than normally and may be delayed The pulses of the ascending aorta are generally larger in valvular than in subvalvular (infundibular) stenosis.

LEFT VENTRICLE. There is prolongation of the ejection phase. both the isometric contraction and the expulsion phase (rapid and delayed) appear prolonged.

LEFT ATRIUM There may be large pulsations due to higher diastolic pressure in the left *ventricle*

Coarctation of the Aorta. Small pulses have been recorded below the point of narrowing, in contrast with the pulses above the narrowing In the majority of the cases, however, normal pulsations have been recorded along the aorta In some cases, the pulses of the intercostal arteries are recorded (Fig 6-39).

The *left ventricular curve* is characterized by large pulsations of normal appearance. The left atrium also shows evidence of increased dynamics.

Ebstein's Disease. In the few cases reported, an increase of pulsations of the right atrium was observed. The presystolic waves were nonobservable, while large positive waves were observed in systole, evidence of tricuspid insufficiency.

Conclusions. The EKy study of congenital heart diseases may provide similar data to those obtained with roentgenkymography. However, the patterns recorded by the former method are more typical and easier to study. The most important data are obtained over the pulmonary artery, hila, and peripheral pulmonary fields, especially in pulmonary hypertension and in cases with abnormal pulmonary flow. However, it is impossible to reach a clinical-anatomic diagnosis of the malformations only on the basis of the functional data revealed by the EKy. The *most typical* patterns are observed in pulmonic stenosis and in shunts (chiefly patent ductus).

Blood in congenital heart disease

MARIO STEFANINI AND FRANCO GOBBI

There are significant changes in morphologic and chemical constituents of the blood in the course of some congenital heart diseases. A review of the literature indicates that this subject has been discussed often but has seldom received adequate treatment.

A few generalizations may be made as introductory remarks *Significant blood changes are found in congenital heart disease only when venous-arterial shunts or other anomalies, important enough to induce cyanosis, are present.* Two findings are outstanding (1) *increased red cell mass* with relative lack of involvement of the other formed elements of the blood; this produces the classic picture of secondary polycythemia, (2) defects in the hemostatic and blood-clotting mechanisms leading to *blood hypocoagulability* and, under certain circumstances, to severe bleeding All changes revert to normal after successful corrective surgery. They will be discussed separately.

SECONDARY POLYCYTHEMIA

The polycythemic state of cyanotic congenital heart disease is a compensatory mechanism to the low arterial blood O_2 saturation and tissue hypoxia. Thus, it is constantly associated with cyanosis and clubbing of the fingers (Fig 6-40) severe dyspnea, etc. The liver and spleen may be palpable in a small number of cases (Lawrence).

Blood findings are those typical of polycythemia of the so-called secondary type (Table 6-3). Erythrocyte count, hemoglobin level, and hematocrit are very high. White cell and neutrophil counts may be slightly above normal but are most often normal; platelets are never above the normal range and are, in fact, dras-



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LEFT VENTRICLE. There is prolongation of the ejection phase: both the isometric contraction and the expulsion phase (rapid and delayed) appear prolonged.

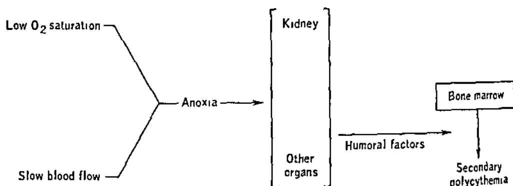
LEFT ATRIUM. There may be large pulsations due to higher diastolic pressure in the left ventricle.

Coarctation of the Aorta. Small pulses have been recorded below the point of narrowing, in contrast with the pulses above the narrowing In the majority of the cases, however, normal pulsations have been recorded along the aorta In some cases, the pulses of the intercostal arteries are recorded (Fig 6-39) The *left ventricular curve* is characterized by large pulsations of normal appearance. The left atrium also shows evidence of increased dynamics.

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Conclusions. The EKy study of congenital heart diseases may provide similar data to those obtained with roentgenkymography. However, the patterns recorded by the former method are more typical and easier to study. The most important data are obtained over the pulmonary artery, hila, and peripheral pulmonary fields, especially in pulmonary hypertension and in cases with abnormal pulmonary flow. However, *it is impossible to reach a clinical-anatomic diagnosis of the malformations only on the basis of the functional data revealed by the EKy. The most typical patterns are observed in pulmonic stenosis and in shunts* (chiefly patent ductus).

DIAGRAM 6-2. MECHANISMS OF SECONDARY POLYCYTHEMIA IN CYANOTIC CONGENITAL HEART DISEASE



Low arterial O_2 saturation, slow blood flow (due to high red cell mass and blood viscosity) cause tissue anoxia Hypoxia of kidney, possibly other organs, causes release of humoral (? hormonal) factors (among which may be erythropoietin), stimulating the bone marrow to high red cell production (secondary polycythemia).

lated with the enormously increased production of erythrocytes, the rapid turnover and utilization of iron over a long period of time, and its relative depletion from tissue stores This consideration would make an intensive program of venesection inadvisable in these patients, unless severe symptoms of congestive heart failure are present. The administration of iron has also been recommended in selected cases where hypochromia is outstanding Iron has been given to children with cyanotic congenital heart disease whose hematocrit is lower than 75. Above this figure, the result of high blood viscosity interferes with the beneficial effects of the O_2 carrying power of an even fully hemoglobinized red cell.

The polycythemia of cyanotic congenital heart disease is alleviated by decreasing the need for O_2 transport. Thus, it decreases when patients are kept at continuous rest. It completely regresses when the responsible mechanical defect is corrected by cardiac surgery.

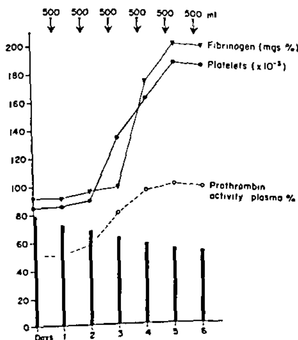


Fig. 6-41. Effect of repeated venesections on platelets, fibrinogen, and plasma prothrombin activity in a patient with Eisenmenger's syndrome and severe cyanosis. Black columns indicate the hematocrit value.

THE COAGULATION DEFECT

Most clinicians agree that patients with cyanotic congenital heart disease frequently present the paradoxical combination of thrombotic and hemorrhagic manifestations. The most common *thrombotic manifestations* involve the lungs, the mesenteric vessels, and the superficial veins They need not be clinically evident, as one may see silent extensive thrombosis of vessels (especially pulmonary), both recent and old, in autopsy material The most frequent and serious complication is the thrombosis of cerebral vessels, followed by sudden *hemiplegia* The combination of high red cell mass, slow blood flow, and high blood viscosity with resulting clumping of erythrocytes and possible clumping of platelets, and the intimal damage due to hypoxia, are among the most significant pathogenic factors (Fig 6-41).

Treatment of thrombotic complications in patients with cyanotic congenital heart disease is beset with difficulties. Anticoagulation with

TABLE 6-3 LABORATORY FINDINGS IN CASE OF FIG 6-40

Urine: Albumin	1 + (20 mg%)
Blood:	
RBC	8 75 M/mm³
Hb	22 5 gm%
Ht.	82 0
Reticulocytes	1.4%
WBC	8,970
Differential count, %	
P	63
E	3
B	1
L	24
M	9
ESR	1 mm/1 hr (Westergren)
Platelets	110,000 mm³ (direct method)
Red cell volume	63 cc/kg weight
Plasma volume	28 7 cc/kg weight
O_2 saturation (arterial)	74%
Serum bilirubin	1 2 mg%
Serum uric acid	4 7 mg%
Serum iron	140γ/100 ml

Bone Marrow:	
Cellularity, +	
Differential count, %	
Megakaryocytes	0 2
Myeloblasts	1 0
Promyelocytes	2.4
Myelocytes	11.3
Eosinophilic myelocytes	0 2
Basophilic myelocytes	0 1
Metamyelocytes	3 2
Band cells	12 3
Neutrophils	15 4
Eosinophils	1.0
Basophils	0 1
Lymphoblasts	0 2
Lymphocytes	5 3
Erythroblasts	4 6
Normoblasts	40 0
Unclassified	1 8

tically reduced in many cases The *total blood volume is very high,* primarily because of the high red cell mass, since the plasma volume is never high and is often reduced [1] Viscosity of whole blood is high, plasma viscosity is normal The reticulocyte count is high, suggesting an accelerated rate of red cell production or destruction No evidence, however, has thus far been submitted of a shortened life span of the erythrocytes in secondary polycythemia. The slight elevation of indirect reacting serum bilirubin, the higher-than-normal serum iron level (in some stages of the disease), and the increased fecal urobilinogen excretion are best explained by the total increased metabolism of hemoglobin due to the polycythemic state, without need of postulating an exaggerated hemolysis The two- to threefold increase in red cell production has been documented by Fe^{59} turnover studies (Lawrence) Moreover, bone marrow studies indicate significant normoblastic hyperplasia, while myeloid elements are only slightly hyperplastic and megakaryocytes are not, as a rule, high in number or activity.

[1] The behavior of the total blood, plasma, and red cell volumes is not standard in different types of cyanotic congenital heart disease (Nelson et al) High red cell mass and low plasma volume are found [illegible] high red cell mass and increased plasma volume as well.

The mechanism of the secondary polycythemia in congenital heart disease with cyanosis is complex (Diagram 6-2). *It is linked* with the low arterial blood O_2 saturation and the resulting *tissue hypoxia*. Figures as low as 30 per cent (or even lower) have been reported (Taussig, 1947a), with most cases showing values from 50 to 75 per cent, which drop considerably with mild exercise or crying An aggravating factor may be the *high blood viscosity,* which causes "sludging" within the small vessels and further reduces blood *flow.* A hypoxic bone marrow reacts with secondary polycythemia, possibly mediated through a humoral agent (Reissman). Tissue hypoxia, however, may lead to polycythemia through other mechanisms as well The authors have recently shown that renal venostasis, induced by unilateral partial ligation of the renal vein in dogs, induces a transitory polycythemic state, which regresses when sufficient collateral circulation has developed (van Lessen et al). This erythrocytotic state may be due to the stimulatory effect of a humoral factor, possibly "erythropoietin," produced in excess under the experimental conditions It is not improbable that hypoxia of other organs as well might have similar stimulatory effects on the bone marrow, as postulated many years ago.

An interesting clinical observation is that most patients with cyanotic polycythemia become relatively *hypochromic* in later stages (Rudolph et al). This finding may be corre-

hours following surgery is a serious complication. For the above reasons, coumarin drugs should be given only in small doses while heparin may be used with less circumspection, provided patient is under observation for the appearance of bleeding manifestations. Full details of anticoagulant treatment are found in Taussig's monograph (1947a).

Patients with cyanotic congenital heart disease also present a well-known *hemorrhagic tendency*, which is similar to that found in polycythemia vera and in hypoxic secondary polycythemia. The bleeding manifestations consist of epistaxis, hemoptysis, hematemesis, cerebral hemorrhages, and spreading ecchymotic areas in the skin Their occurrence has been described as "high" by Hartman

A clue to the mechanism of hemorrhage in these patients is the behavior of the *erythrocyte sedimentation rate*, which is very low, normally less than 5 mm/1 hr by the method of Westergren, and often as low as 0 Together with high blood viscosity and high red cell mass, other factors must be present to explain such a low erythrocyte sedimentation rate. One of these factors is the severe fibrinogenopenia of these patients

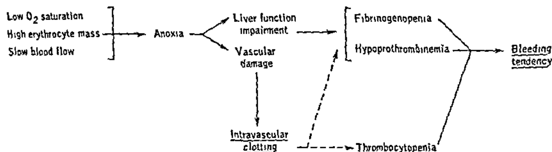
Fibrinogen deficiency, however, is only a facet of the breakdown of the hemostatic process through a complex mechanism (Diagram 6-3). The *tourniquet test* is often positive, possibly because of the damaging effects of hypoxia on the vessel walls The *clotting time* determined in silicone-coated test tubes may be slightly prolonged *Clot retraction* is impaired because of a variety of causes which include fibrinogenopenia, poor production of thrombin, and low plasma with high red cell volumes. The most important factors are probably the high red cell mass and the inability of the reduced fibrinogen to hold red cells into a firm clot Thus, the retraction of a plasma clot is adequate. When, however, whole blood is observed, the poor fibrin mesh is unable to hold on to the red cell mass Two phenomena may then become apparent either the clot shrinks rapidly and sinks to the bottom of the test tube, or the clot appears as a small knob at the blood-air interspace, while most of the red cell mass is at the bottom of the tube The clot retraction is quickly corrected (1) in vitro, with the dilution of blood, and (2) in vivo, with the reduction of the red cell mass and the correction of the hematocrit to normal values by means of venesections. An additional mechanism in the defect of clot retraction may be the thrombocytopenia which has been observed in some of these patients.

An analytic study of the various clotting factors and of tests which give an over-all indication of the adequacy of the coagulation process supplies many interesting results, which, in the experience of the authors may be summarized as follows: (1) decreased activity of the antihemophilic globulin (AHG) and of the plasma thromboplastic component (PTC); (2) true hypoprothrombinemia and, possibly, decreased activity of accessory factors of prothrombin conversion, (3) sharp decrease in the concentration of fibrinogen[3] The patient's serum accelerates the generation of thromboplastin when added to normal platelets and plasma, thus suggesting the presence of clotting accelerator factors. There are no anticoagulants, but at least in the experience of the authors, fibrinolytic and antifibrinolytic activity are increased.

The interpretation of these findings is a moot question. They are not due to technical artefacts. There is also no evidence that deficient absorption of vitamin K is involved in the pathogenesis of the hypoprothrombinemia As already suggested, the defective protein synthesis by an anoxic liver is a real possibility Without minimizing this factor, the authors believe, however, that intravascular clotting, due to sludging and anoxia of the vascular wall, may be of primary importance in the pathogenesis of the hemostatic defect (as well as of the thrombotic tendency) in cyanotic congenital heart disease (Diagram 6-3). The low concentration and activity of factors leading to the formation of thrombin, the thrombocytopenia, and the evidence of activation of the fibrinolytic mechanism, at times found in these patients, could follow the occurrence of intravascular clotting. Additional evidence is the appearance of clotting accelerators in these patients' serum Also, patients with cya-

[3] Such findings remain significant, even after proper correction is made for the excess of anticoagulant due to the low plasma volume, and in the case of prothrombin and accessory factors, for the low fibrinogen level, also when calcium added for the performance of the various tests is adjusted to the increased concentration of the anticoagulant

DIAGRAM 6-3 PATHOGENETIC MECHANISMS OF THE COMBINED HEMORRHAGIC AND THROMBOTIC TENDENCY IN CYANOTIC CONGENITAL HEART DISEASE



re- [illegible]

[illegible]

coumarins in full doses appears contraindicated because of the hypersensitivity of these patients to such drugs,[3] even though they also exhibit a latent hemorrhagic tendency. Only cautious doses of Dicumarol or analogues can be considered, with careful control of the plasma prothrombin time and of possible hemorrhagic manifestations (nasal mucosa, skin, urine) Heparin may be used in standard doses, with careful control of the clotting time and frequent examination of the patient for signs of clinical bleeding.

Thrombosis, especially of the cerebral vessels, becomes of greater impact following corrective cardiac surgery, as it apparently occurs in 3 to 4 per cent of all cases (Favre-Gilly et al) These figures are probably unrealistic, since they are based on data which were not always checked by autopsy, but they are still significant enough to indicate the magnitude of this problem. Prevention and treatment of this surgical complication present many difficulties The thrombotic tendency of these patients, however, is well correlated with their blood viscosity This is nearly twice as high (9 to 11 times that of water) as in normal blood (5 to 6 times) (Isaacs).

In the experience of the authors, no operation should be attempted in these patients unless their hematocrit has been reduced to a level at which the blood viscosity is nearer to normal This may not always be possible, but in any case, venesections carried out until the patient notices an increase of dyspnea have been proved to reduce the evidence of postsurgical thrombotic complications This is a somewhat debatable point, and the individual experience of the surgeon should be the most important factor in deciding how much and how quickly blood should be removed.

The authors routinely remove two-tenths to three-tenths of the calculated blood volume in a period of a few days, at the rate of 1 pint (500 ml) a day or less, depending on the age of the patient. The volume withdrawn is replaced with freshly collected plasma. The incidence of thrombotic complications seems lessened by the use of this approach. Venesection is also followed by a rise in the platelet count, plasma fibrinogen level, and prothrombin activity, when these are low (Diagram 6-3). Thus, the hemostatic mechanism reverts to a state of relative normality as the clot retraction, number of platelets, and coagulation mechanism become adequate, while the possibility of hemorrhagic complications is reduced as well.

The occurrence of thrombosis in the

[3] The hypoxia of the liver seems accompanied by impairment of function, which may cause a relative inhibition of the synthesis of prothrombin Such hypothesis is supported by the finding that these patients have poor BSP excretion, which reverts to normal when venesections reduce the hematocrit to near normal values Coumarin drugs, in any case, have a more rapid, severe, and prolonged anticoagulant effect in these patients.

hours following surgery is a serious complication. For the above reasons, coumarin drugs should be given only in small doses while heparin may be used with less circumspection, provided patient is under observation for the appearance of bleeding manifestations. Full details of anticoagulant treatment are found in Taussig's monograph (1947a).

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notic congenital heart disease who died at surgery and showed a severe hemostatic breakdown during life present occasionally intravascular deposition, especially in the smaller pulmonary vessels, of material resembling fibrin (Beaumont and Bourgain). Finally, it has been observed that the concentration of fibrinogen and the activity of plasma prothrombin in these patients may change rapidly from day to day, possibly in relation to the extent of a process of continuous intravascular clotting.

The hemorrhagic tendency becomes of greater significance during and after surgical procedures The tendency of these patients to bleed after dental extractions, tonsillectomies, or even minor cuts and abrasions is well known. More serious bleeding manifestations are encountered when corrective cardiac surgery is carried out Fatal hemorrhage occurs in about 15 per cent of patients with congenital heart disease in the few days following cardiac surgery (Potts, Taussig et al., 1951) The figures are at least three times higher in the experience of European surgeons (Favre-Gilly et al.) *Usually, bleeding does not occur during surgery, rather in the immediate postoperative course* The pathogenesis of such severe bleeding is not altogether clear Of particular interest in this respect is a patient (Beaumont and Bourgain) who bled fatally following the repair of an atrial septal defect with pulmonary stenosis. Blood was uncoagulable and fibrinogen level was very low; yet, at postmortem, the smaller pulmonary vessels showed both old, partly recanalized, and recent thrombi. This finding again suggested that incoagulability of the blood might have been the end result of intravascular coagulation

The prevention of the occurrence of fatal hemorrhage in the course of, and after, corrective cardiac surgery is based on reducing the red cell mass by venesections, with or without replacement by plasma or fibrinogen. *In the practice of the authors, patients with primary or secondary polycythemia who are scheduled for surgery are routinely venesected to an almost normal hematocrit and transfused with* normal plasma. Hemorrhagic and thrombotic complications have become almost obsolete with this technique. The experience of the authors with cases of cyanotic congenital heart disease, unfortunately more limited, suggests *the same approach.* This method of preventive treatment has been fully described in the discussion of the prevention of the thrombotic accidents

Cardiac catheterization in congenital heart disease

ALFRED P. FISHMAN
AND A. GREGORY JAMESON

INTRODUCTION

Intubation of the human heart is currently accomplished by three routes: (1) venous, (2) retrograde arterial, and (3) direct cardiac. Of the three, venous catheterization of the right heart has been most extensively applied to the diagnosis of congenital heart disease (Bing, 1952; Cournand et al., 1949, 1953, Burchell et al., 1948, Dexter et al., 1947; Donzelot et al., 1954, Edwards et al, Gotzsche et al.; Keith et al; Zimmerman), it has been used to provide (1) mixed venous blood for the calculation of cardiac output by the Fick principle, (2) blood samples for the estimation of flow through intracardiac shunts; (3) central venous sites for the injection of tracer substances for the calculation of cardiac output and central blood volume, (4) direct recordings of mechanical and electrical events, and heart sounds from within the cardiac cavities; and (5) a channel for the intracardiac injection of contrast material for the roentgen visualization of intracardiac structures and channels of flow.

It is pertinent to stress at this point that cardiac catheterization is no substitute for an adequate clinical examination. Indeed, the technique is most rewarding when preliminary examinations focus the attention of a skilled team on the types of defect which may be anticipated.

Nature of the Defects Generally Encountered in Congenital Heart Disease. In general, there are four types of cardiovascular abnormalities which may be encountered by the probing catheter: (1) an abnormal communication between contiguous cardiac chambers and/or adjacent vessels, (2) a stenosis or atresia of a normal valvular communication between consecutive chambers, (3) anomalous origins or insertions of major vessels, and (4) combinations of 1, 2, and 3.

Physiologic Basis for Evaluation of Data Obtained by Venous Catheterization. Some aspects of the normal circulation warrant emphasis with respect to the interpretation of data obtained by cardiac catheterization in patients with congenital heart disease:

Within the first few days of life, there is functional closure of the ductus arteriosus and the foramen ovale (Born et al); the pulmonary circulation is thereby separated from the systemic circulation This postnatal separation of the two circulations may be demonstrated by the combination of arterial oximetry and the intravenous injection of the blue dye T 1824 (Burchell, 1950); a curve depicting the change in dye concentration at the arterial site is free of evidence for either intrapulmonary recirculation or the early entry of dye into the systemic arterial circulation

In the normal heart, the average cardiac outputs of both sides of the heart are, under steady-state conditions, approximately equal In the presence of intracardiac communications, valvular insufficiency, or extensive bronchial collateral circulation, this balance may

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[illegible]

monary vessels, of material resembling fibrin (Beaumont and Bourgain). Finally, it has been observed that the concentration of fibrinogen and the activity of plasma prothrombin in these patients may change rapidly from day to day, possibly in relation to the extent of a process of continuous intravascular clotting.

The hemorrhagic tendency becomes of greater significance during and after surgical procedures The tendency of these patients to bleed after dental extractions, tonsillectomies, or even minor cuts and abrasions is well known. More serious bleeding manifestations are encountered when corrective cardiac surgery is carried out Fatal hemorrhage occurs in about 1.5 per cent of patients with congenital heart disease in the few days following cardiac surgery (Potts, Taussig et al, 1951). The figures are at least three times higher in the experience of European surgeons (Favre-Gilly et al). *Usually, bleeding does not occur during surgery; rather in the immediate postoperative course* The pathogenesis of such severe bleeding is not altogether clear. Of particular interest in this respect is a patient (Beaumont and Bourgain) who bled fatally following the repair of an atrial septal defect with pulmonary stenosis. Blood was incoagulable and fibrinogen level was very low, yet, at postmortem, the smaller pulmonary vessels showed both old, partly recanalized, and recent thrombi. This finding again suggested that incoagulability of the blood might have been the end result of intravascular coagulation.

The prevention of the occurrence of fatal hemorrhage in the course of, and after, corrective cardiac surgery is based on reducing the red cell mass by venesections, with or without replacement by plasma or fibrinogen. In the practice of the authors, patients with primary or secondary polycythemia who are scheduled for surgery are routinely venesected to an almost normal hematocrit and transfused with normal plasma. Hemorrhagic and thrombotic complications have become almost obsolete with this technique. The experience of the authors with cases of cyanotic congenital heart disease, unfortunately more limited, suggests the same approach. This method of preventive treatment has been fully described in the discussion of the prevention of the thrombotic accidents

TABLE 6-5. NORMAL VALUES FOR THE OXYGEN CONTENT OF BLOOD SAMPLES WITHDRAWN FROM THE CENTRAL VEINS AND RIGHT HEART

Location	*O_2 content, ml 100 ml*	*O_2 saturation,* per cent*
Inferior vena cava	15.8	80
Superior vena cava	15.0	76
Right atrium: coronary sinus	9.4	47
Right atrium: tricuspid area	15.3	78
Right ventricle	15.5	79
Pulmonary artery	15.5	79

* Per cent oxyhemoglobin saturation as determined spectrophotometrically or calculated from Van Slyke analysis as

$$\frac{O_2 \text{ content} - \text{dissolved } O_2}{O_2 \text{ capacity} - \text{dissolved } O_2} \times 100$$

abnormal communication between the two circulations will establish pressure gradients for left-to-right flow. In Table 6-4 are listed representative normal values for each circulation.

The pulmonary artery pressure is little affected by large increments in pulmonary vascular flow (Cournand), acute hypoxia generally affects larger increments in pressure (5 to 10 mm Hg) with only slight increases in blood flow. Experiments with acute hypoxia in normal subjects (Fishman et al.) have emphasized the pitfalls entailed in translating a change of resistance of a vascular bed (measured as pressure drop divided by blood flow) into a change of vasomotor activity.

Pulmonary artery and right ventricular systolic pressures are virtually identical, at rest and during exercise, even with dilatation of the pulmonary artery, unless there is a narrowing which creates a gradient between them.

Each chamber and vessel has a characteristic pressure pulse, as well as pressure level. In some instances, as in the case of the left and right atria, these may be sufficiently different to be of diagnostic aid (Fig. 6-42).

If a communication is established between the two circulations, the degree of shunting will depend, in large part, on the relative sizes of both the defect and the normal channels. If the defect is sufficiently small, it may constitute almost the entire resistance to flow, on the other hand, as it approaches the normal outlet in size, resistances distal to the defect may largely determine the degree of shunting. Thus, flow through a congenital ventricular septal defect having the same size as the aortic outlet is largely a function of the degree of stenosis of the pulmonic valve and of the anatomic alterations in the pulmonary vascular bed.

In the normal subject, the intact cardiac septa and the closed ductus arteriosus separate the arterialized blood, contained in the left heart and aorta, from the venous blood in the right heart and pulmonary artery. In the presence of an abnormal communication, the pressure gradients between adjacent structures will favor the addition of arterialized blood to venous blood unless the normal relation of pulmonary to systemic resistance has been reversed. Attempts to upset this balance physiologically, as by acute hypoxia which raises pulmonary artery pressure (Burchell et al.), are of more hemodynamic than diagnostic interest. In Table 6-5 are listed representative values for the oxygen content of blood sampled from the great veins and right heart of a normal subject, as indicated in this table, venous blood achieves complete mixing and uniform composition at the level of the right ventricle and pulmonary artery.

The comparison of the oxygen content of samples consecutively withdrawn from consecutive cardiac chambers is valid only in the face of a stable state of the respiration and circulation. In this state, the oxygen contents of each chamber remain relatively constant, in changing states, such as may occur during anesthesia or excitement, blood pressures, flows, and oxygen contents may be constantly changing, complicating not only the comparison of the oxygen content of consecutive samples but also the interpretation of oximeter blue-dye curves.

INFORMATION OBTAINED BY CARDIAC CATHETERIZATION

The Course of the Catheter. The most direct evidence for the presence of a congenital cardiac defect is the fluoroscopic demonstration of an abnormal course of the cardiac catheter (Cournand et al., 1953). This evidence may become difficult to interpret in an enlarged, abnormal heart; in such cases, aid

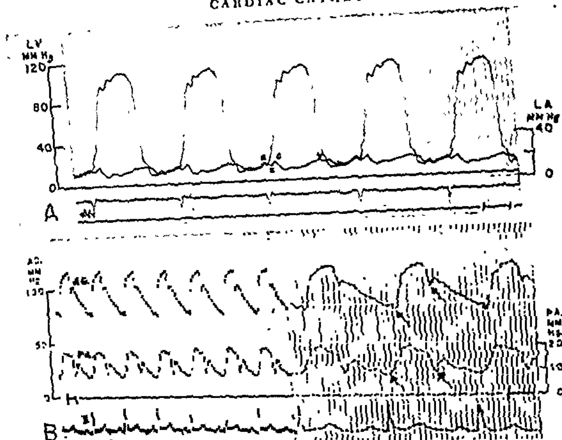


Fig 6-42. A. Simultaneous left ventricular (LV) and left atrial (LA) pressure pulses in a patient with normal circulation. The positive waves (a, c, v) and the negative wave (z) of the normal left atrial pressure pulse are indicated. B. Simultaneous aortic (AO) and pulmonary artery (PA) pressure pulses in a patient with normal circulation. The paper speed is 25 mm/sec on the left and 75 mm/sec on the right. Time lines are 0.04 sec apart. Arrows indicate the beginning of ejection and end of protodiastole in the aorta and pulmonary artery (Braunwald, Fishman, and Cournand)

be upset, effecting a different volume-work load on the two ventricles

Immediately following the physiologic closure of the ductus arteriosus, blood pressures in the pulmonary circulation approximate those in the systemic circulation. Within a few weeks, despite the continued output of equal blood volumes by both ventricles, adult blood pressure relationships are established; these are characterized by lower blood pressures in the right ventricle and pulmonary artery than in their systemic counterparts[1] (Table 6-4). The drop in vascular resistance and blood pressure in the pulmonary circulation is associated with the transition of prenatal thick-walled, small muscular arteries into thin-walled adult vessels (Edwards, 1953). The left atrial mean blood pressure also exceeds the right atrial mean pressure. Consequently, if the pulmonary circulation undergoes its normal postnatal evolution, an

Table 6-4. Normal Blood Pressures in the Pulmonary and Systemic Circulations

Location	Systolic	Diastolic, mm Hg	Mean
Right atrium	...	..	3
Right ventricle	25	2	
Pulmonary artery	25	9	15
Pulmonary "wedge"	...	..	6
Left atrium	...	..	5
Left ventricle	120	4	
Aorta	120	80	92

[1] See Part 4, Chap 12, for normal data. Editor.

formed intracavitary pressure pulses; e.g., tricuspid insufficiency characteristically alters the right atrial pressure pulse (Fig. 6-44); (2) abnormal pressure gradients across valves (Fig. 6-45); (3) pressure pulses similar to those of the left heart chambers recorded during right heart catheterization (Fig. 6-46); (4) abnormal levels of intracardiac blood pressure, these have to be interpreted in the light of other observations. Thus, right ventricular systolic hypertension may reflect increased resistance to outflow posed by a stenotic pulmonic orifice, by pulmonary vascular changes, or by free communication between the right ventricle and the systemic circulation via a large interventricular septal defect, an elevated end-diastolic pressure in the right ventricle establishes right heart failure but does not define the cause. Some characteristic values for intracardiac blood pressures in congenital heart disease are illustrated in Table 6-6.

Intracardiac Variations in Blood Oxygen Content. A left-to-right shunt may be recognized by detecting the admixture of arterialized blood to the venous blood traversing the

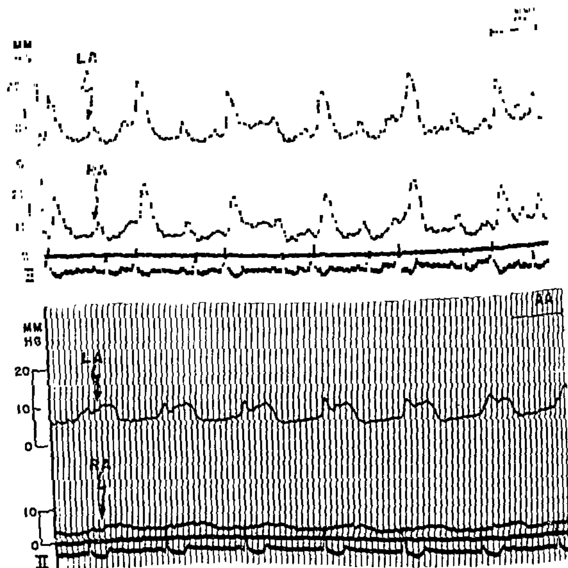


Fig. 6-44. (Upper) Pressure pulses recorded from the left atrium (*LA*) and right atrium (*RA*) prior to circumferential ligature of the atrial septal defect. The similarity in the left and right atrial pressure pulses is consistent with a large defect. The pressure pulses are *distorted* by high peaks which accompany functional insufficiency of the AV valves during premature ventricular beats. (Lower) Immediately following closure of the defect, the right atrium became a flaccid bag; the pressure pulse (*RA*) is devoid of characteristic contour. On the other hand, the contour of the left atrial pressure pulse (*LA*) is consistent with a functional insufficiency of the mitral valve; this insufficiency pattern is ascribable to the nodal rhythm.

in localization may be afforded by recording characteristic blood pressures and pressure pulses from the tip of the catheter. Highly specialized techniques such as intracavitary electrocardiography or phonocardiography may occasionally be of help, the role of selective angiocardiography is discussed below. X-rays illustrating the course and position of the cardiac catheter in various types of congenital heart disease are reproduced in Fig 6-43, below

The Intracardiac Pressure Pulses. Four types of abnormalities may be encountered in the intracardiac blood pressures. (1) de-

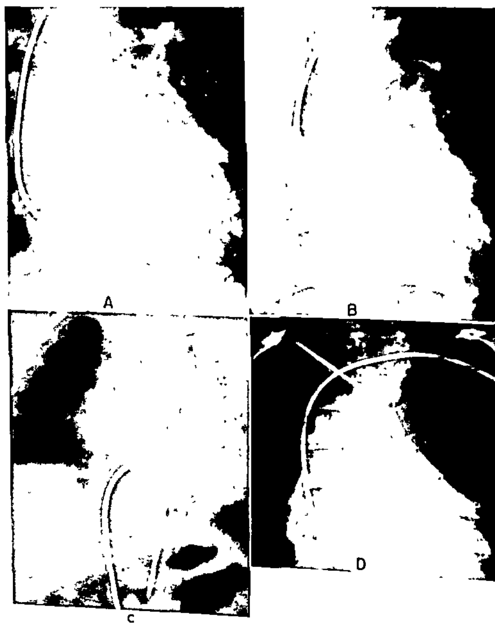


Fig. 6-43. A. Normal route traversed by the cardiac catheter The tip is located in the right pulmonary artery. B The catheter has traversed an atrial septal defect. The tip is lodged in the left atrium C The catheter has passed from the left pulmonary artery through a patent ductus arteriosus to the descending aorta. D. The catheter has crossed a ventricular septal [illegible] and passed via the aorta into the right innominate arter[illegible] recording [illegible]

formed intracavitary pressure pulses; e.g., tricuspid insufficiency characteristically alters the right atrial pressure pulse (Fig. 6-44); (2) abnormal pressure gradients across valves (Fig. 6-45), (3) pressure pulses similar to those of the left heart chambers recorded during right heart catheterization (Fig. 6-46); (4) abnormal levels of intracardiac blood pressure; these have to be interpreted in the light of other observations. Thus, right ventricular systolic hypertension may reflect increased resistance to outflow posed by a stenotic pulmonic orifice, by pulmonary vascular changes, or by free communication between the right ventricle and the systemic circulation via a large interventricular septal defect, an elevated end-diastolic pressure in the right ventricle establishes right heart failure but does not define the cause. Some characteristic values for intracardiac blood pressures in congenital heart disease are illustrated in Table 6-6.

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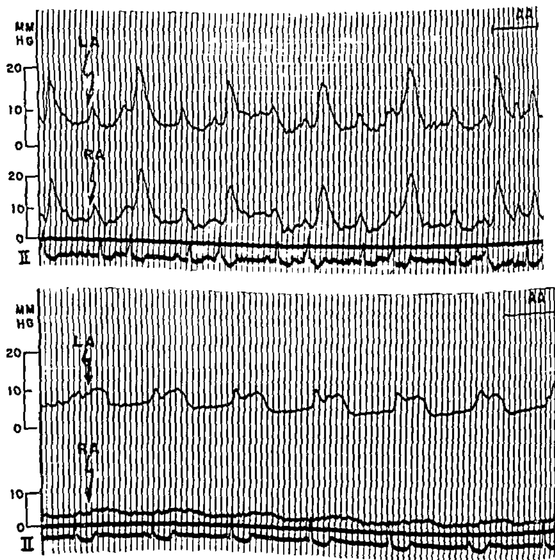


Fig. 6-44. (Upper.) Pressure pulses recorded from the left atrium (*LA*) and right atrium (*RA*) prior to circumferential ligature of the atrial septal defect The similarity in the left and right atrial pressure pulses is consistent with a large defect The pressure pulses are distorted by high peaks which accompany functional insufficiency of the AV valves during premature ventricular beats. (Lower.) Immediately following closure of the defect, the right atrium became a flaccid bag; the pressure pulse (*RA*) is devoid of characteristic contour On the other hand, the contour of the left atrial pressure pulse (LA) is consistent with a functional insufficiency of the mitral valve; this insufficiency pattern is ascribable to the nodal rhythm

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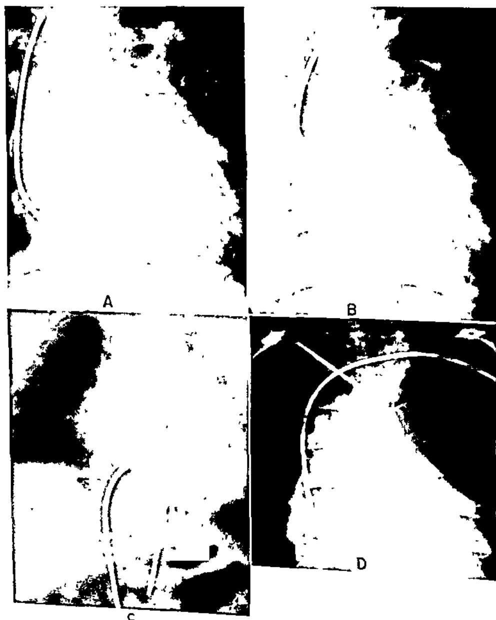


Fig 6-43. A Normal route traversed by the cardiac catheter. The tip is located in the right pulmonary artery B. The catheter has traversed an atrial septal defect The tip is lodged in the left atrium. C. The catheter has passed from the left pulmonary artery through a patent ductus arteriosus to the descending aorta D The catheter has crossed a ventricular septal defect and passed via the aorta into the right innominate artery [illegible] recording [illegible] ... ed by

nical skill is available for reliable oximetry and for the analysis of individual blood samples and if the volume of blood required for both procedures is not excessive. A large increment in oxygenation, which persists in samples obtained from multiple sites within and distal to a chamber, suggests a large shunt. However, there are several considerations which limit the equation of an increment in oxygen content to a left-to-right shunt. (1) the observed increment must exceed analytic error and must not reflect incomplete mixing of normal converging streams, e.g., the vena cava and coronary sinus in the right atrium; (2) the respiration and circulation must be sufficiently stable so as to avoid spontaneous fluctuations in oxygen content between successive samplings, this is particularly difficult to accomplish in anesthetized patients, and (3) other types of congenital anomalies, such as insertion of pulmonary veins into the right atrium, which may be responsible for abnormal increments in oxygen content must be excluded. The latter situation is especially troublesome in the case of atrial septal defects since these are frequently associated with anomalous insertions of pulmonary veins into the right atrium.

The possible errors mentioned under (1), above, as well as other possible errors due to sampling, handling, or analysis of the specimens, can be minimized by statistical evaluation of the analytic results, e g , by comparison of the average values from the different chambers by the "t test." The sensitivity of the statistical result increases as the number of samples increases. Spectrophotometric methods of blood analysis permit the use of many samples without excessive blood loss, except in the smallest infants, and provide highly accurate results. Indeed, when multiple small samples from successive chambers are analyzed spectrophotometrically and the mean values are statistically compared by the "t test," the sensitivity of shunt detection is of the same order of magnitude as that obtained with the use of the test gases other than oxygen (Grayzel and Jameson, unpublished data).

Other possible sources of confusion warrant brief mention. Thus, a small atrial defect with left-to-right shunt may be missed and a ventricular septal defect may be erroneously di-

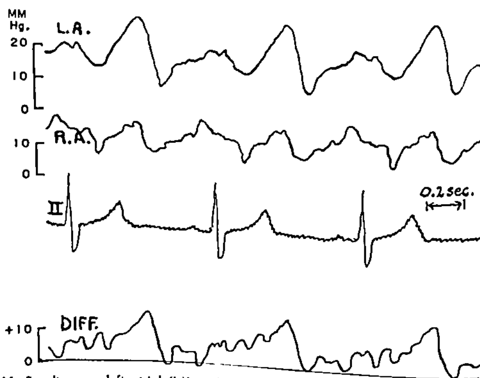


Fig. 6-46. Simultaneous left atrial (LA), right atrial (RA), and differential atrial (DIFF) pressure curves in a subject with normal circulation. Note the high V point in the left atrial pressure pulse. The differential pressure curve demonstrates that the left atrial pressure exceeds the right atrial pressure virtually throughout the entire cardiac cycle. *(Braunwald, Fishman, and Cournand.)*

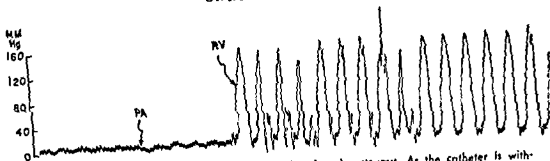
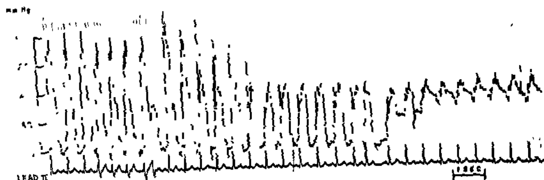


Fig. 6-45. A Characteristic pressure pulses in pulmonic valve stenosis. As the catheter is withdrawn from the pulmonary artery (PA), the low, distorted pulmonary artery pressure pulse is abruptly succeeded by a right ventricular (RV) pattern. The right ventricular systolic hypertension contrasts sharply with the level of blood pressure in the pulmonary artery.



B Characteristic pressure pulses in subvalvular aortic stenosis. As the catheter is *withdrawn* from the body of the left ventricle past the *subvalvular stenosis, the high systolic pressure* is reduced abruptly to an abnormally low pressure in the infundibular *chamber. There* is no further change in the systolic pressure as the catheter is withdrawn across the aortic valve into the aorta.



C. Hydrogen curves *recorded simultaneously* with platinum-tipped catheters from the *pulmonary* artery and the brachial artery in a *patient* with a left-to-right shunt at the ventricular level After the patient inhales gaseous hydrogen, the appearance of the gas in the right side *of the heart* sooner than in the peripheral *artery signals* the presence of a left-to-right shunt at or proximal to the position of the intracardiac sampling site.

central systemic veins, the right heart, or the pulmonary artery. Two techniques are generally used, either singly or in combination: *cuvette oximetry* for rapid estimation of oxyhemoglobin saturation of blood *sampled from consecutive* cardiac chambers and vessels and the more tedious determination of oxygen content or oxyhemoglobin saturation in *individual* blood samples by *the Van Slyke* or *spectrophotometric methods*; the latter are *generally* completed after the cardiac *catheter* has been withdrawn

There is little question that a combination of the two is most rewarding if adequate tech-

TABLE 6-6. REPRESENTATIVE DATA OBTAINED BY CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE (*Continued*)

	Diagnostic location of catheter	*Blood pressure*			*Blood samples*		
					O_2 content		*O_2 saturation* *
		Right ventricle	*Pulmonary artery*	*Right atrium*	*Right ventricle*	*Pulmonary artery*	*Systemic artery*
			Cyanotic Patients				
Patent ductus arteriosus, with reversal of flow	Left pulmonary artery to aorta	.	Exceeds systemic blood pressures		.	Exceeds right ventricle	Considerably decreased, particularly in femoral artery
Tetralogy of Fallot	Overriding aorta; left ventricle	Systolic hypertension,† systolic blood pressure equals aortic	Low blood pressure; pulse distorted		Exceeds right atrium	.	Considerably decreased
Large ventricular septal defect	Overriding aorta; left ventricle	Systolic hypertension,† systolic blood pressure equals aortic	Same systolic pressure as in right ventricle			.	Considerably decreased

* Determined directly by spectrophotometry or from Van Slyke analysis as

$$\frac{O_2 \text{ content} - \text{dissolved } O_2}{O_2 \text{ capacity} - \text{dissolved } O_2} \times 100$$

† [illegible]

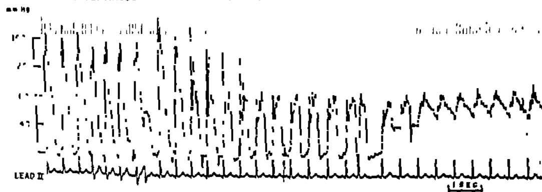
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(Clark and Bargeron) Similar principles govern the use of oxygen and these other test substances for the identification of a left-to-right shunt. The nitrous oxide method appears to be somewhat less sensitive than the other three. The radioactivity of the krypton and the ethyl iodide is a possible drawback to their use. The hydrogen method has the advantage of requiring no blood samples (Fig. 6-45C).

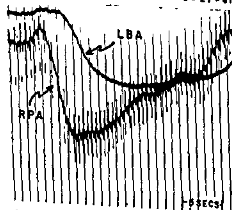
Oxygen Unsaturation of Hemoglobin in Arterial Blood. In unanesthetized patients with congenital cardiac defects, systemic arterial hemoglobin unsaturation reflects the admixture of venous to arterial blood. Despite extensive pulmonary vascular lesions, diffusion limitation for oxygen apparently contributes little to the systemic arterial hypoxemia. The type of peripheral arterial unsaturation which results from venous-arterial admixture is generally not relieved by breathing 100 per cent oxygen. Localization of the site of the veno-arterial shunt generally requires methods other



Fig. 6-45 A. Characteristic pressure pulses in pulmonic valve stenosis. As the catheter is withdrawn from the pulmonary artery (*PA*), the low, distorted pulmonary artery pressure pulse is abruptly succeeded by a right ventricular (*RV*) pattern. The right ventricular systolic hypertension contrasts sharply with the level of blood pressure in the pulmonary artery.



B. Characteristic pressure pulses in subvalvular aortic stenosis. As the catheter is withdrawn from the body of the left ventricle past the subvalvular stenosis, the high systolic pressure is reduced abruptly to an abnormally low pressure in the infundibular chamber. There is no further change in the systolic pressure as the catheter is withdrawn across the aortic valve into the aorta.



C Hydrogen curves recorded simultaneously with platinum-tipped catheters from the pulmonary artery and the brachial artery in a patient with a left-to-right shunt at the ventricular level After the patient inhales gaseous hydrogen, the appearance of the gas in the right side of the heart sooner than in the peripheral artery signals the presence of a left-to-right shunt at or proximal to the position of the intracardiac sampling site.

central systemic veins, the right heart, or the pulmonary artery. Two techniques are generally used, either singly or in combination: *cuvette oximetry* for rapid estimation of oxyhemoglobin saturation of blood sampled from consecutive cardiac chambers and vessels and the more tedious determination of oxygen content or oxyhemoglobin saturation in individual blood samples by the *Van Slyke* or *spectrophotometric methods;* the latter are generally completed after the cardiac catheter has been withdrawn.

There is little question that a combination of the two is most rewarding if adequate tech-

Although these formulas for pulmonary and systemic blood flow are in general use, they add little to the clinical and fluoroscopic evidence for increased or decreased pulmonary blood flow. Ridiculous values may result from inadequate sampling of mixed venous blood. The formulas also become totally inadequate in the presence of large systemic collateral flow to the lungs.

Estimation of the Degree of Stenosis and the Size of Intracardiac Defects. Considerable insight as to the functional significance of the stenosis of a semilunar valve may be gained from a clinical appraisal of the degree of hypertrophy and dilatation of the respective ventricle; in the case of pulmonic stenosis, this clinical evidence is supported by the demonstration of right ventricular systolic hypertension by cardiac catheterization. Cardiac catheterization may also provide some indirect evidence as to the size of a defect, thus, in the case of a left-to-right shunt, a large defect is suggested by sampling highly oxygenated blood over a wide area in a right heart chamber; this evidence for a large shunt may be supported by pulmonary hypertension and a wide pulmonary artery pulse pressure

In the case of a right-to-left shunt, a large venoarterial communication is suggested by a considerable degree of systemic hypoxemia, the degree of venous admixture may be estimated from a simple mixing formula which calculates the volume of mixed venous blood which must be added to fully oxygenated pulmonary venous blood in order to obtain the observed peripheral arterial oxyhemoglobin saturation (Burchell, 1950). In the presence of large venoarterial shunts (greater than 27 per cent of the pulmonary blood flow), the hemoglobin of systemic arterial blood generally remains unsaturated despite the breathing of 100 per cent oxygen

A more direct method has been developed for estimating the size of a septal defect, this entails the use of a balloon-tipped catheter which is inflated in situ with radiopaque material to delineate the diameter of the defect, this method has also been used to estimate the volume flow through the defect by comparing the oxygen content of blood defect, it has also been used to estimate the volume flow through the defect by comparing the oxygen content of blood sampled in the vicinity of the defect, prior to and following functional obliteration of the abnormal communication (Kjellberg et al., 1950).

Limitations in the Interpretation of the Results. Although considerable information may be gained from cardiac catheterization, there are several limitations which are inherent in its application to congenital heart disease (1) the catheter may fail to enter an area of stenosis, or an abnormal communication, or an anomalous origin or insertion of a great vessel; (2) the degree of shunting may be so small as to escape detection on the basis of blood gas analyses; (3) multiple shunts or complex defects involving atrial and ventricular cavities may be difficult to identify, and (4) estimates of blood flow through the pulmonary circulation may, in the face of intracardiac shunts, be totally erroneous These deficiencies may generally be overcome by appropriate use of complementary diagnostic methods.

ATRIAL SEPTAL DEFECT

The presence of an atrial septal defect may be identified by introducing the catheter into the left atrium during right heart catheterization (Cournand et al., 1949, 1953). If such a defect is suspected prior to catheterization, it may be desirable, particularly in children, to catheterize a vein of the lower, rather than the upper, extremity, since traversal of an atrial septal defect is apparently facilitated by entering the heart via the venous stream from below (Lind and Wegelius). However, this gain in approach to the atrial defect sacrifices the ease in entering the pulmonary artery via an upper extremity route

The entry of the catheter into the left atrium may be established by (1) further advancing the catheter into a pulmonary vein or the left ventricle, (2) recording typical left atrial pressure pulses, and (3) withdrawing blood samples which are enriched in oxygen content as compared to samples drawn from the venae cavae.

The sampling of arterialized blood from the right atrium does not identify an atrial septal defect Similar samples may be obtained when there is anomalous insertion of pulmonary veins into the right atrium, distinction between these two anomalies is complicated by the frequent association of atrial septal defects with anomalous insertions of the pulmonary veins *Other causes for arterialization of right atrial*

agnosed if the oxygenated stream is first encountered in the right ventricle, a ventricular septal defect may also be suggested by the regurgitation of oxygenated blood through an insufficient pulmonary valve in a patient with a patent ductus arteriosus and pulmonary hypertension. Finally, the incorrect diagnosis of patent ductus arteriosus may be proposed on the basis of oxygenated blood withdrawn from a catheter advanced almost to a wedge position.

The Use of Test Gases Other than Oxygen for the Detection of Left-to-Right Shunts. Recent work to improve the sensitivity and speed of shunt detection has led to the introduction of four inhalants: nitrous oxide (Morrow), radioactive krypton (Sanders), radioactive ethyl iodide (Case et al.), and hydrogen

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		Blood pressure			*Blood samples*		
	Diagnostic location of catheter	*Right ventricle*	*Pulmonary artery*	*Right atrium*	*O_2 content* — *Right ventricle*	*O_2 content* — *Pulmonary artery*	*O_2 saturation* * — *Systemic artery*
Normal subject		22/2 mm Hg (average)	22/9 mm Hg (average)	No greater than highest vena cava	Same as right atrium	Same as right ventricle	96% (average)
				Acyanotic Patients			
Pulmonic *stenosis*	Normal	Systolic hypertension †	Low blood pressure; pressure pulse distorted	. . .	. .	. .	Slightly decreased if complicated by a patent foramen ovale
Atrial septal defect	Left atrium	. .	. . .	Exceeds both vena cava ‡	. .	. .	Often slightly decreased due to transient reversal of atrial pressure gradient
Small ventricular septal defect	Left ventricle and aorta	.	. .	. . .	Exceeds right atrium		
Patent ductus arteriosus	Aorta	.	. . .	. . .	. . .	Exceeds right ventricle	

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than cardiac catheterization, such as angiocardiography or the combination of cardiac catheterization and other specialized techniques, such as multiple injections of test substances at various sites within the heart. Arterial unsaturation of one segment of the body may be of diagnostic value, thus, in a patent ductus arteriosus with reversal of flow, *greater unsaturation of femoral than the right brachial artery blood generally occurs.*

The Venous Injection of Dye Combined with Arterial Oximetry. This procedure has most value in right-to-left shunts which are identified by short appearance times and abnormal initial deflections (Wood, 1953, Burchell, 1950) Two types of additional information may be obtained: (1) localization of the site of the defect, this involves the sequential injection of dye into consecutive cardiac chambers, and (2) an estimate of the partition of blood flow between the normal and abnormal routes.

The combination of venous injection of dye and arterial oximetry is also of value in establishing the existence of a left-to-right shunt; its particular value in identifying the anomalous insertions of pulmonary veins will be discussed

[illegible]

tions in oxyhemoglobin saturation which are involved in the use of T-1824

Selective Angiocardiography. This technique involves the rapid introduction of radiopaque material into the heart through the cardiac catheter for demonstration of intracardiac structures and patterns of blood flow (Kjellberg et al, 1950). It is particularly valuable for delineating venoarterial communications and for accurate definition of the site and nature of a cardiac defect. The procedure entails some hazard, particularly in cyanotic patients and in patients who are given multiple injections, it also requires specialized equipment for its performance. Since the information obtained depends on the site of injection of the contrast material, some preliminary screening is necessary for most fruitful yield from this technique

Relative Blood Flows through the Pulmonary and Systemic Circulations. In the absence of an abnormal communication, blood flow through the lungs and systemic circulation is approximately equal and may be estimated by the Fick method; this entails the simultaneous measurement, in a steady state (Fishman et al.), of the oxygen uptake at the mouth in conjunction with the corresponding arterial-mixed venous blood oxygen difference For the calculation of pulmonary blood flow in the face of a left-to-right shunt, blood is assumed to be completely mixed in the chamber distal to the site of communication, and the hemoglobin in pulmonary venous blood is assumed to be fully, or almost fully, saturated with oxygen The following simple formulas are commonly used for the estimation of the relative blood flows through the pulmonary and systemic circulations and through the abnormal communications (Bing).[2]

Systemic flow (ml/min)

$$= \frac{O_2 \text{ uptake (ml/min)} \times 100}{\left[\left\{\begin{matrix}O_2 \text{ content of peripheral arterial} \\ \text{blood (ml/100 ml)}\end{matrix}\right\} - \left\{\begin{matrix}O_2 \text{ content of mixed venous} \\ \text{blood (ml/100 ml)}\end{matrix}\right\}\right]}$$

Pulmonary artery flow (ml/min)

$$= \frac{O_2 \text{ uptake (ml/min)} + 100}{\left[\left\{\begin{matrix}O_2 \text{ content of pulmonary vein} \\ \text{blood (ml/100 ml)}\end{matrix}\right\} - \left\{\begin{matrix}O_2 \text{ content of pulmonary artery} \\ \text{blood (ml/100 ml)}\end{matrix}\right\}\right]}$$

Effective pulmonary flow (ml/min)

$$= \frac{O_2 \text{ uptake (ml/min)} \times 100}{\left[\left\{\begin{matrix}O_2 \text{ content of pulmonary vein} \\ \text{blood (ml/100 ml)}\end{matrix}\right\} - \left\{\begin{matrix}O_2 \text{ content of mixed venous} \\ \text{blood (ml/100 ml)}\end{matrix}\right\}\right]}$$

Over-all shunt (left to right) = pulmonary artery flow − systemic flow

Over-all shunt (right to left) = systemic flow − pulmonary artery flow

Total left-to-right shunt = pulmonary capillary flow − effective pulmonary flow

Total right-to-left shunt = systemic flow − effective pulmonary flow

In these formulas, *effective pulmonary blood flow* represents the volume of blood which, after returning to the right atrium, reaches the pulmonary capillaries

55

[2] [illegible] 2 *Editor.*

more than a few millimeters of mercury in a patient with left-to-right atrial shunt would suggest organic pulmonic stenosis. However, the use of the pressure gradient for the estimation of the degree of stenosis is handicapped by the abnormally high transvalvular flows.

When an atrial septal defect is associated with mitral stenosis, it may be possible to introduce the catheter into the left ventricle in order to demonstrate a diastolic pressure gradient across the mitral valve.

VENTRICULAR SEPTAL DEFECT

Cardiac catheterization generally clinches the clinical diagnosis of a ventricular septal defect and provides an index of its hemodynamic significance.

The most certain evidence for a ventricular septal defect is the introduction of the catheter from the right into the left ventricle or aorta; the fluoroscopic and x-ray evidence (Fig. 6-43) is then reinforced by obtaining samples of highly oxygenated blood from the tip of the catheter and by recording the transition from the high (left ventricular) to the lower (right ventricular) pressures as the catheter is withdrawn

The catheter frequently fails to enter the left heart or aorta However, the withdrawal of highly oxygenated blood samples from the right ventricle coupled with the clinical and electrocardiographic data are usually sufficient to establish the diagnosis. Only on rare occasions is it necessary to resort to additional techniques such as elective angiocardiography or the demonstration of abnormally brief circulation times for dye injected into the right ventricle.

An increase in oxygenation in the right ventricle must be interpreted in the light of clinical data; thus, similar increments may be caused by laminar flow from an atrial septal defect, a perforated aneurysm of the sinus of Valsalva, or pulmonary insufficiency in association with a patent ductus arteriosus and pulmonary hypertension. Exceedingly small defects may escape detection if they fail to provide a significant increase in oxygenation of right ventricular blood or if they establish a right ventricular stream which is not sampled by the catheter.

Cardiac catheterization may also provide some insight as to the size of the defect. A defect smaller than the pulmonary valve orifice does not interfere with the functional separation of the two ventricles; the normal difference between right and left ventricular systolic blood pressures is therefore maintained. In the absence of pulmonic stenosis, the *presence of a higher blood pressure in the right ventricle than in the systemic circulation* suggests the combination of (1) a small ventricular septal defect, (2) a greater resistance to flow in the lesser circulation than in the systemic circulation, and (3) the absence of an overriding aorta.

A large defect equalizes blood pressure in both ventricles. In this circumstance, the partition of flow between systemic and pulmonary circulations depends upon the relative resistance to outflow posed by the two circulations; adequate perfusion of systemic structures may be accomplished at the expense of a decreased pulmonary blood flow if there is stenosis of the outflow tract of the right ventricle or if there are anatomic alterations in the pulmonary vascular bed. In the face of a fixed anatomic resistance in the lesser circulation, transient increases in the right-to-left flow may be accomplished by systemic vasodilator agents.

Pulmonary and right ventricular systolic and diastolic hypertension may accompany a ventricular septal defect, particularly in children. However, systemic hypoxemia due to a right-to-left shunt does not occur until systolic blood pressure in the pulmonary artery exceeds that in the systemic arteries.

A high septal defect allows passage from the right ventricle into the aorta, consequently, the entry of the catheter into the aorta from the right ventricle fails to distinguish between a high septal defect and an overriding aorta.

Such considerations have led some investigators (Selzer, Selzer and Laqueur, Becu et al.) to regard Eisenmenger's complex as a physiologic variant of a large ventricular septal defect, without pulmonic stenosis The gradual evolution of persistent cyanosis is then ascribable to a progressive increase in pulmonary vascular resistance to blood flow, which ultimately leads to a right-to-left ventricular shunt. This explanation is consistent with the concept that the pulmonary vascular lesions of Eisenmenger's complex represent an anatomic response to increased vascular blood flow and pressures rather than a congenital abnormality of blood vessels It also implies

and afford an index of its severity; (2) localize the site of the obstruction, i.e., valvular, infundibular, or both, and (3) establish the coexistence of other congenital anomalies.

The hallmark of pulmonic stenosis is a *systolic pressure gradient between right ventricle and pulmonary artery.* Some insight into the site and anatomic nature of the stenosis may be gained from a correlation of the distance traversed by the catheter and the nature of the pressure pulses. Thus, an abrupt change in blood pressure level and contour as the catheter crosses the pulmonic valve suggests a valvular stenosis Figure 6-45 demonstrates systolic hypertension in the right ventricle, a distorted, damped hypotensive blood pressure in the pulmonary artery, and a sharp zone of transition between the two chambers

By way of contrast, an example of infundibular stenosis is illustrated in Fig. 6-47. The record displays a series of intermediate complexes which persisted over the length of the right ventricular outflow tract during withdrawal of the catheter These intermediate complexes have systolic pressure peaks equal to those in the pulmonary artery, whereas the diastolic pressures correspond to those in the right ventricle. In other instances of infundibular stenosis (Bouchard and Cornu), the intermediate complexes may be distorted by systolic dips to subzero levels, these distortions have been ascribed to *venturi effects* elicited by jets of blood through the stenotic area during ventricular ejection. Particular emphasis is generally placed on the shape of the distorted pulmonary artery pressure pulse in identifying pulmonic stenosis On rare occasions, despite severe stenosis, a normal pulmonary artery pressure pulse has been recorded (Fig 6-47). In this instance, the preservation of normal contour and blood pressure is probably related to an augmented pulmonary vascular flow occasioned by an associated left-to-right shunt.

These criteria, based on analysis of blood pressure records, generally suffice to identify the nature of the stenosis. Occasionally, particularly in the case of complex anomalies, they may be misleading. Thus, venturi distortions have also been recorded from an infundibular chamber (Torner-Soler et al). Moreover, in the case of combined valvular and infundibular stenosis (Fig 6-48), the infundibular pattern may emerge only after the valvular stenosis has been surgically relieved.

Cardiac catheterization also provides an objective index of surgical accomplishment (Milstein and Brock, Kirklin et al) (Fig 6-49). In general, a surgical attack upon the pulmonic valve decreases right ventricular systolic pressure and increases pulmonary artery pressures, but only rarely is the systolic pressure gradient between right ventricle and pulmonary artery completely abolished. It has recently been demonstrated that improvement in the blood pressures and pressure pulses may continue long (i.e., months to a year) after surgery (Himmelstein et al.); this has been interpreted as a reflection of a gradual diminution in the subvalvular muscle mass after relief of the obstruction to right ventricular outflow On occasion, a pulmonary insufficiency pattern may appear (Fig. 6-50)

Despite severe stenosis, pulmonary blood flow may be normal at rest and during exercise. A change in transvalvular flow may affect the pressure drop across the stenotic area. Thus, a decrease in cardiac output may diminish, whereas an increase in cardiac output may augment, the gradient. In practice, it has

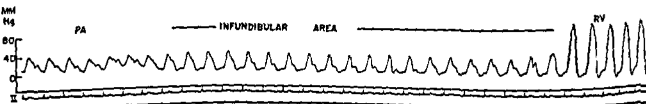


Fig. 6-47. Withdrawal of the cardiac catheter from the pulmonary artery (PA) into the right ventricle (RV) in a patient with combined infundibular stenosis and atrial septal defect. The transitional complexes are characterized by systolic blood pressures equal to those in the pulmonary artery and diastolic blood pressures equal to those in the right ventricle. The normal pulmonary artery pressure pulses are discussed in the text. *(From unpublished data of Himmelstein, Jameson, Humphreys, and Fishman.)*

that the degree of aortic overriding is only of minor hemodynamic significance.

SINGLE VENTRICLE

The course of the catheter may demonstrate the origin of the aorta and pulmonary artery from a common ventricular chamber. The ventricular blood pressures and the oxygen content of blood samples are consistent with a large ventricular septal defect, the oxygen content of blood samples from the ventricle is far in excess of those drawn from the right atrium

Associated malformations of the great vessels and of the AV valves may complicate interpretation of data obtained during cardiac catheterization. A rudimentary outlet chamber may [illegible]

unless the mouth of the other vessel is stenosed. Considerable insight into the nature of the associated defects may be gained from selective angiocardiography.

PATENT DUCTUS ARTERIOSUS

In the majority of children and young adults, clinical evidence is sufficient to establish the diagnosis of a patent ductus arteriosus. Cardiac catheterization has its greatest value in patients with atypical murmurs Two types of supportive evidence are frequently adduced during cardiac catheterization. (1) the venous catheter may identify the ductus arteriosus by entering the channel between the left pulmonary artery and the aorta, (2) blood samples drawn from the pulmonary artery have a higher oxygen content than do samples from the right ventricle

The distinction between a patent ductus arteriosus and an aortopulmonary septal defect is of surgical interest Cardiac catheterization may be of some help in this regard if particular attention is paid to the course of the catheter, thus, the passage of the catheter along the aortic arch, or its entry, without angulation, into the right common carotid artery suggests an aortopulmonary septal defect rather than a patent ductus arteriosus.

In some patients, particularly those with large communications, pulmonary artery hypertension develops (Hultgren et al.; Storstein and Helle). In these subjects, pulmonary vascular resistance may continue to increase, and pulmonary artery blood pressures may equal or even exceed systemic artery pressures (Fig. 6-51). The left-to-right shunt is then reversed and venous blood flows from the pulmonary artery into the aorta, causing peripheral arterial oxyhemoglobin unsaturation. In the case of identical pressures in both circulations, with virtually no flow across the ductus, the balance may be upset by decreasing systemic vascular resistance. This may be accomplished in a variety of ways (Burchell et al, 1948), including exercise and inhalation of amyl nitrite; the reversal of flow is then revealed by systemic oxyhemoglobin unsaturation. When reversal of flow is established, the dye-dilution curve of a left-to-right shunt is replaced by the characteristic double-humped contour of a right-to-left shunt. Of considerable diagnostic value at this time is the comparison of the oxygen content in blood samples simultaneously drawn from the femoral and right brachial arteries. In the presence of a patent ductus arteriosus with right-to-left shunt, the femoral arterial blood sample may be less saturated with oxygen than the brachial. The anatomic basis for this difference is illustrated in Fig. 6-52. This difference is another basis for distinction from an aortopulmonary window with right-to-left shunt

Since the abnormal communication is usually not traversed by the catheter, the supportive evidence for a patent ductus arteriosus often resolves into differences between the oxygen content of blood samples successively drawn from the right ventricle and pulmonary artery. This criterion may fail to distinguish between a high ventricular septal defect and a combination of patent ductus arteriosus with left-to-right shunt, pulmonary hypertension, and pulmonary insufficiency. Conversely, a high ventricular septal defect with laminar flow of oxygenated blood into the pulmonary artery may lead to the erroneous diagnosis of a patent ductus arteriosus In such troublesome cases, selective angiography or retrograde aortography may become necessary for identification of the anomaly.

PULMONIC STENOSIS

Cardiac catheterization may provide several types of information with respect to pulmonic stenosis (Dow et al, 1950; Green et al.; Maraist et al; Pollack et al.; Silber et al.). It may (1) identify the presence of an obstruction to outflow from the right ventricle

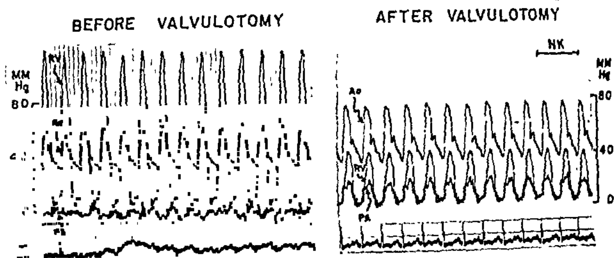


Fig. 6-50. The effect of valvulotomy and extensive resection of the infundibular area in a patient with pulmonic stenosis. The operation has accomplished a striking reduction in right ventricular (RV) systolic blood pressure. Pulmonary artery (PA) systolic blood pressure has returned to normal. The identical diastolic blood pressures in the right ventricle and pulmonary artery indicate pulmonary insufficiency. (From unpublished data of Himmelstein, Jameson, Humphreys, and Fishman)

possible mechanism for such a gradient is an abnormally large transvalvular blood flow, as may occur in a left-to-right shunt. However, theoretical considerations suggest that the pressure differences required to move large volumes of blood across a normal pulmonary valve are exceedingly small, this concept is supported by the absence of measurable differences between right ventricular and pulmonary artery systolic pressures either during severe exercise (cardiac output two to three times normal) or in hyperkinetic disease states associated with large volume flows.

Considerations such as these suggest that a systolic pressure gradient greater than a few millimeters of mercury reflects organic pulmonic stenosis, as a practical measure, to allow for artefacts in blood pressure recording

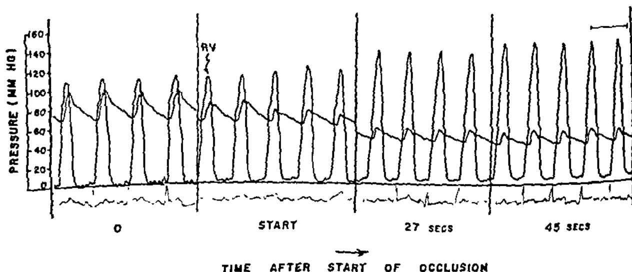


Fig. 6-51. Simultaneous blood pressures in the right ventricle and aorta in a patient with patent ductus arteriosus and reversal of flow. Records taken at the time of operation by direct puncture. Prior to closure of the ductus, pulmonary artery systolic blood pressure exceeds the aortic. Following occlusion, the right ventricular systolic blood pressure increases further and aortic blood pressures drop as the flow of blood into the aorta via the ductus is interrupted. By 45 sec, right ventricular diastolic blood pressures have increased considerably, reflecting the onset of right heart failure. These changes promptly were reversed when the occluding ligature was released. (From unpublished observations of Jameson, Sirak, Humphreys, and Fishman)

that the degree of aortic overriding is only of minor hemodynamic significance.

SINGLE VENTRICLE

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Associated malformations of the great vessels and of the AV valves may complicate interpretation of data obtained during cardiac catheterization. A rudimentary outlet chamber may give origin to the aorta, or pulmonary artery, or both. In general, the vessel originating from the rudimentary chamber has the lower blood flow unless the mouth of the other vessel is stenosed. Considerable insight into the nature of the associated defects may be gained from selective angiocardiography.

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tricle may not be encountered. The resistance to outflow imposed by the pulmonic valve is fixed, whereas resistance to flow through the systemic circulation is determined by the state of the systemic arterioles; consequently, the balance of ventricular pressures may be upset by systemic vasodilatation, resulting in an augmentation of the right-to-left shunt and an exaggeration of systemic hypoxemia (Hamilton et al., 1950).

Various indices have been used to estimate the degree of dextroposition of the aorta. The course of the catheter is of little help since a high ventricular defect permits entry into the aorta even if there is no measurable degree of overriding. Other tests, such as the demonstration of abbreviated right-ventricle-to-ear circulation times, are unreliable. The most clear-cut demonstration of the origin of the aorta is by selective angiocardiography (Kjellberg et al., 1955)

The estimation of the volume of pulmonary blood flow by the Fick principle is particularly unreliable in this anomaly since (1) shunts complicate the sampling of mixed venous blood, and (2) the pulmonary capillaries may be perfused by systemic arterial blood as well as by pulmonary artery blood. Generally, an estimate of the ratio of systemic to pulmonary blood flow is attempted by the following type of calculations.

Systemic blood flow

$$= \frac{\text{oxygen uptake (ml/min)} \times 100}{\left\{\begin{array}{l}\text{systemic artery } O_2 \text{ content (ml/100 ml)} \\ \quad - \text{right atrial } O_2 \text{ content (ml/100 ml)}\end{array}\right\}}$$

Maximum pulmonary blood flow

$$= \frac{\text{oxygen uptake (ml/min)} \times 100}{\left\{\begin{array}{l}\text{pulmonary venous } O_2 \text{ content (ml/100 ml)} \\ \quad - \text{systemic artery } O_2 \text{ content (ml/100 ml)}\end{array}\right\}}$$

Minimum pulmonary blood flow

$$= \frac{\text{oxygen uptake (ml/min)} \times 100}{\left\{\begin{array}{l}\text{pulmonary venous } O_2 \text{ content (ml/100 ml)} \\ \quad - \text{pulmonary artery } O_2 \text{ content (ml/100 ml)}\end{array}\right\}}$$

Pulmonic stenosis and an atrial septal defect may mimic a tetralogy of Fallot. Selective angiocardiography has been found particularly useful in distinguishing between these combinations of defects (Kjellberg et al., 1955). On the other hand, the association of an atrial septal defect and the tetralogy of Fallot is not uncommon (Esclavissat et al.). The atrial defect may consist only of a patent foramen ovale which is accidentally traversed by the catheter or may be sufficiently large to constitute a source of a large right-to-left shunt when right atrial pressures increase.

ANOMALOUS INSERTIONS OF PULMONARY VEINS

Partial Anomalous Drainage. The diagnosis of anomalous drainage of pulmonary veins into a central systemic vein may be established from the route traversed by the catheter during central venous catheterization, it may be confirmed by demonstrating arterialized blood at the site of insertion of the anomalous vessels into the systemic veins. Cardiac catheterization may be similarly rewarding when a pulmonary vein inserts into the right atrium, particularly in the case of a vein from the right lung (Hickie). However, an erroneous diagnosis may stem from the inadvertent passage of the catheter across an atrial septal defect into the mouth of a pulmonary vein as it inserts normally into the left atrium.

Once the presence of anomalous pulmonary vein has been established, it is of surgical interest to determine whether there is an associated atrial septal defect. This problem may not be easy to resolve by cardiac catheterization unless the course of the catheter fortuitously identifies both abnormalities, the oxygen contents of blood samples from the right atrium are of no avail in this regard; nor are hemodynamic measurements of diagnostic aid since each defect alone (as well as both together) increases pulmonary blood flow and may increase pulmonary artery pressures.

In some instances, insight as to the functional significance and anatomy of anomalously inserted pulmonary veins, either alone or in combination with an atrial defect, may be gained from the nature of the curves recorded by arterial oximetry following injection of a dye into successive cardiac chambers. Occasionally, when there is a fortunate anatomic circumstance of completely normal drainage from one lung combined with completely abnormal drainage from the other, the separate injection of blue dye into each pulmonary artery may identify the abnormality. Unfortunately, the dye-dilution method is least rewarding in the usual types of anomalous insertion, as well as in the frequent combination of anomalous pul-

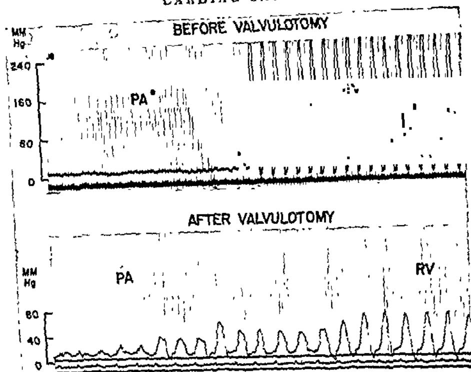


Fig 6-48 Withdrawal of the catheter from the pulmonary artery (PA) into the right ventricle (RV) in a patient with combined valvular and infundibular stenosis. Before valvulotomy, the pattern is characteristic of valvular stenosis After valvulotomy, the pattern of infundibular stenosis emerges (*From unpublished data of Himmelstein, Jameson, Humphreys, and Fishman*)

been established that a wide gradient, measured under the usual conditions of cardiac catheterization, reflects a hemodynamically significant degree of pulmonic stenosis. Moreover, it appears that such a gradient is not obscured by the alterations in respiration and circulation which attend anesthesia and surgical manipulation prior to the attack on the pulmonic valve (Himmelstein et al.).

The question has been repeatedly posed as to whether a systolic pressure gradient may occur without organic pulmonic stenosis; one

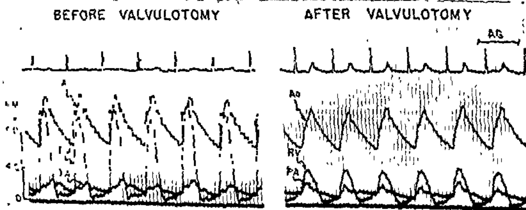


Fig 6-49. The effect of valvulotomy on right heart and systemic blood pressures in a patient with pulmonary valvular stenosis The blood pressures were recorded by needle puncture prior to, and following, valvulotomy *Each record* displays the ECG, the aortic (AO), right ventricular (RV), and pulmonary artery (PA) pressure *pulses* Valvulotomy has reduced, but has not completely abolished, the systolic pressure gradient across the pulmonic valve The ECG has reverted to normal (*From unpublished data of Himmelstein, Jameson, Humphreys, and Fishman*)

hypertension and an elevated pulmonary "wedge" pressure may reflect left heart failure.

Arterial catheterization reveals a characteristic distortion of the pressure pulse as the catheter traverses the stenotic area. Injection of contrast medium proximal to the stenotic area may outline the area of stenosis.

PRIMARY PULMONARY HYPERTENSION

The value of cardiac catheterization lies in (1) establishing the existence and degree of pulmonary hypertension and (2) excluding congenital heart disease and back pressure from the left heart as its basis. The effect of ganglionic blocking agents in lowering pressures in the pulmonary circulation is of physiologic interest but of no diagnostic value.

CORRECTED TRANSPOSITION OF THE GREAT VESSELS

Catheterization may be of help in the diagnosis of corrected transposition Because of the altered anatomy, the catheter may take an intracardiac course suggestive of the diagnosis. The abnormal positions and relations of the atrioventricular and semilunar valves account for the unusual intracardiac courses that may be taken by the catheter. A malformation of the left atrioventricular valve, such as that seen in Ebstein's disease, is not rare (Schiebler et al.).

Pressures in the right heart in a patient without septal defect or valvular deformity studied by one of the authors (A.G.J) were entirely normal. This observation emphasizes the point that by itself the anomaly of corrected transposition does not produce significantly altered hemodynamics. With associated defects, pressures and shunts are compatible with the associated anomalies and their severity.

Selective angiocardiography offers the most help in making the diagnosis.

TRANSPOSITION OF GREAT VESSELS

Complete Transposition. Cardiac catheterization generally contributes little to the diagnosis of complete transposition of the great vessels (Campbell and Suzman) To be of diagnostic value, the catheter should enter all four cardiac chambers for the recording of blood pressures and the withdrawal of blood samples. In practice, this feat is exceedingly difficult to accomplish. Most often the catheter is advanced from the right ventricle into the aorta, establishing from its course that the aorta arises anteriorly in the position usually occupied by the pulmonary artery (Gotzsche)

Cardiac catheterization is of most value in identifying the nature and direction of flow in coexisting shunts. This estimation of the degree of shunting is generally based on variation in the oxygen content of blood samples withdrawn from successive cardiac chambers. Unfortunately, the interpretation of the degree of shunting from these data is usually complicated by apparently unpredictable variations in the magnitude, and even direction, of shunt.

Incomplete Transposition. In incomplete transposition of the great vessels (Taussig-Bing complex), cardiac catheterization may be more definitive (Taussig and Bing; Martin and Lewis). The catheter may enter both the aorta and pulmonary artery from the right ventricle. Because of the high ventricular septal defect, systolic pressures of both ventricles as well as both great vessels are identical. Systemic hypoxemia is generally marked, and considerable diagnostic value has been ascribed to the greater degree of oxygenation of blood in the pulmonary artery than in a systemic artery. Pulmonary blood flow is increased except in the case of associated pulmonic stenosis. Selective angiocardiography offers considerable promise in defining the origin of the great vessels as well as the nature of the associated anomalies (Kjellberg et al.).

ENDOCARDIAL FIBROELASTOSIS

The pressure pulses in the right ventricle and atrium may resemble those of constrictive pericarditis (Fig. 6-53) due to decreased diastolic expansion of the ventricles imposed, in this instance, by a constrictive endocardial sclerosis (McKusick and Cochran). In practice, particularly in infants and children, this distinctive pattern is generally not manifest.[3]

AORTIC STENOSIS

Surgical attack on aortic stenosis is now common. It is desirable in planning operation to know the nature and severity of the obstruction Except for the difference in the site of obstruction, there appears to be no significant clinical or hemodynamic difference between the

[3] See also special chapter for this topic: Part 16, Chap 12 *Editor*

and "catheter whip," *a gradient in excess of 10 to 15 mm Hg may generally be accepted as evidence of organic pulmonic stenosis.* Moreover, in the case of complex anomalies, in which there are alternate routes for egress of blood from the right heart, even a small transpulmonary gradient may reflect severe pulmonic stenosis, if the balance of outflow resistances is such as to deviate blood away from the fixed high resistance at the pulmonary valve area

The end-diastolic pressure in the right ventricle may remain normal despite systolic blood pressures in excess of 200 mm Hg, *an increase in end-diastolic pressure above 5 to 7 mm Hg, in a resting subject, is generally associated with systemic evidence of right heart failure.* Incipient failure of the ventricle may be demonstrable only by an elevation of the end-diastolic pressure to abnormal levels *during exercise.* The systolic blood pressure in the right ventricle is of prognostic import only in that sustained, severe ventricular hypertension imposes a work load that may ultimately cause the heart to fail

In the absence of an abnormal venoarterial communication, arterial oxyhemoglobin saturation remains normal, and as long as heart failure is absent, dye dilution curves are normal. As end-diastolic pressures in the ventricle rise, particularly with the advent of heart failure, right atrial pressures also increase, in such a circumstance, an incompletely sealed foramen ovale may, as the normal atrial pressure gradient is reversed, become the site of a right-to-left atrial shunt

Pulmonary stenosis is often associated with atrial or ventricular septal defects. A small patent foramen ovale may be manifested only by slight systemic arterial oxyhemoglobin unsaturation (Selzer et al, 1949), larger atrial defects are more readily detected, in the customary manner, during cardiac catheterization

When pulmonic stenosis is associated with a large ventricular septal defect, the right ventricular and brachial artery systolic pressures are approximately equal, the recording of a right ventricular systolic blood pressure in excess of systemic is evidence against an overriding aorta or a large ventricular septal defect, since these defects cause both ventricles to empty against a common peripheral resistance and fix blood pressures at approximately equal levels (Soulié et al.).

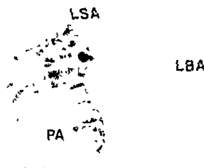


Fig. 6-52. The anatomic basis for comparing the oxygen contents of right brachial and femoral artery blood in the diagnosis of patent ductus arteriosus with reversal of flow. The left subclavian artery may originate, as in this case, opposite the aortic insertion of the ductus arteriosus, 1 sec after retrograde injection into the left brachial artery (LBA), the contrast material has traversed the left subclavian artery (LSA) and the patent ductus arteriosus (not visualized) to enter the pulmonary artery (PA); with such an anatomic arrangement, in the event of reversal of flow, the left brachial and the femoral arteries receive venous blood from the ductus arteriosus, whereas the right brachial blood is normally saturated (From unpublished data of Blumenthal and Ellis)

One complication of cardiac catheterization in pulmonic stenosis warrants brief mention. In severe stenosis, the entry of the catheter into the pulmonary valve may completely arrest right heart output; this is manifested by the prompt onset of cyanosis and circulatory collapse Fortunately, this complication is extremely rare. It is generally completely reversible if the catheter is promptly withdrawn.

TETRALOGY OF FALLOT

Cardiac catheterization in patients with this condition is directed toward the detection of a combination of defects. pulmonic stenosis, high ventricular septal defect, and overriding aorta. The pulmonic stenosis is either infundibular or both infundibular and valvular (Fig. 6-47) The ventricular septal defect is generally large and manifests itself in two ways: (1) by equal systolic blood pressures in the right ventricle and the systemic arteries, and (2) as a channel for access to the aorta from the right ventricle.

Since ventricular pressures are virtually identical, abnormal increments in the oxygen content of blood sampled from the right ven-

monary veins plus atrial septal defect (Swan et al, 1953). Selective angiocardiography may be of some value in these circumstances (Kjellberg).

Complete Anomalous Drainage. This anomaly epitomizes the value of a preliminary able clinical assessment for the most fruitful application of the catheterization technique (Keith et al.), this preliminary appraisal defines the vascular and cardiac sites from which blood may be sampled for comparison of oxygen content. The catheter may outline, as it advances, the course of an anomalous vein, its entry into a common pulmonary venous channel, and finally, its insertion The diagnosis of complete anomalous pulmonary venous return into the more common sites (i e, superior vena cava, right atrium, or inferior vena cava) is then established by (1) withdrawing highly oxygenated blood from the site of confluence, (2) sampling somewhat less oxygenated blood from a systemic artery, and (3) sampling unsaturated blood from a systemic venous channel en route to the pulmonary venous channels.

These data may be supported by dye-dilution curves, which generally indicate pulmonary recirculation, the return of all right ventricular blood to the right atrium, and a right-to-left atrial shunt (Swan and Wood, 1953). If contrast substance is injected at strategic sites, selective angiocardiography may demonstrate the anomalous veins and the pattern of intracardiac blood flow (Kjellberg et al, 1955)

Pulmonary hypertension may accompany the large increment in pulmonary blood flow

EBSTEIN'S DISEASE

Cardiac catheterization plays an important role in establishing this diagnosis (Kilby et al, Kjellberg et al.) The anatomic deformity of the tricuspid valve may complicate or even preclude passage of the cardiac catheter beyond the right atrium The catheter enters a large right atrium which overlaps the normal [illegible] by a wide coil of catheter during attempts to enter the diminutive right ventricle

Simultaneous recording of the intracardiac electrocardiogram and the pressure pulse while the catheter lies in the ventricular portion of the atrium demonstrates an atrial pressure curve and an intraventricular electropotential The combination is accounted for by the presence of ventricular muscle in the atrial wall.

Blood pressure in the right atrium may be increased on account of tricuspid insufficiency, altered characteristics of the right atrial wall, and right heart failure. In any event, an increase in right atrial pressure may establish a right-to-left shunt at the atrial level. The catheter tends to slip back from the diminutive right ventricle, which appears to be like an appendage to the huge right atrium. Blood pressures in the right ventricle and pulmonary artery are normal or low; with the advent of right heart failure, end-diastolic pressure in the right ventricle increases Pulmonary blood flow is low.

Cardiac catheterization in Ebstein's disease may cause various complications. Propensity to runs of atrial and ventricular premature beats suggest a heightened myocardial irritability. Peripheral emboli (Baker et al.) and death (Blacket et al.) have also occurred during the procedure

PERSISTENT TRUNCUS ARTERIOSUS

Cardiac catheterization may demonstrate a large ventricular septal defect. The catheter may leave the right ventricle to enter a wide vessel which is continuous with the aortic arch. If the pulmonary branches are sufficiently large, it may be possible to introduce the catheter into one of them The systolic blood pressure in the ventricles, the arterial trunk, and the pulmonary artery is equal. There is some degree of systemic arterial hypoxemia which is aggravated by exercise.

TRICUSPID ATRESIA

Cardiac catheterization generally adds little to the clinical diagnosis. The catheter cannot enter the right ventricle by the normal route, it is usually deviated through an interatrial septal defect into the left atrium, it may then enter the common ventricle from which highly oxygenated blood may be sampled These observations do not distinguish tricuspid stenosis from tricuspid atresia; selective angiocardiography offers most promise in this regard and in the definition of associated anomalies

COARCTATION OF THE AORTA

Right heart catheterization has no diagnostic value except to exclude associated anomalies such as a patent ductus arteriosus Pulmonary

Certain extra precautions for protection of patient and physician are, therefore, important. These include adequate dark accommodation before proceeding *with the study, the use of protective gloves* by the examiner and of aprons by all observers in the room, and adjustment of the fluoroscope shutters so that only the structures under examination are in the field. Additional shielding of the patient's lower abdomen and genitalia is recommended. Maximum settings of the fluoroscope, especially for milliamperage, should be determined and not exceeded. A clock in the fluoroscopy room, which measures the time that the fluoroscope is actually in use, serves as a check on the physician's fluoroscopy practices and a reminder to improve his technique, so that he can obtain the maximum amount of information in the briefest possible fluoroscopy time.

Since most of the patients with congenital heart disease who undergo these radiographic studies are in the pediatric age group, a few words about handling the infant, toddler, and preschool child may be in order. Securing their cooperation is perhaps the most important phase of the study. The time it takes to establish rapport with the young patient is usually time well spent in terms of the results desired: a satisfactory examination. The barium swallow is most apt to be the objectionable part of the examination. No one likes the chalky taste of this mixture, but it can be made quite palatable by the addition of enough sugar and cocoa. Its consistency should be such that it can be swallowed with ease, yet is thick enough to outline the esophagus while the patient is quickly rotated from one position to another. Thus one swallow is sufficient.

Of the age groups involved, the toddler and preschool child are the most likely to present difficulties in cooperation. It is not hard to conceive that the dark fluoroscope room, the strange noises, the big machine, and the curious attire of the examiners in goggles, aprons, and gloves can be unsettling, at least, if not thoroughly frightening. The advent of television has somewhat simplified the preparation of the child for fluoroscopy, since the fluoroscope screen does resemble that of a television set, and it is customary to view television in a darkened room. Gentle handling by the examiner and the presence of a parent in the room help to get the preschool child satisfactorily through the procedure. Similar technique applies when x-rays are obtained.

Young infants present fewer problems in cooperation than those aged 1 to 4 or 5 years. Best results are obtained when the baby is rested and not hungry and when a pacifier or bottle is available to secure a quiet and relaxed infant for the examination. The baby is less apt to struggle and cry if he is held by the hips for positioning than if his legs, arms, and head are forcibly restrained during the examination.

Children of school age are generally reasonable and cooperative when given an explanation of the *purpose of the studies and* what is expected of them.

The manner of performance and interpretation of these studies should be systematic, though the technique will vary with the examiner.

The following description is one that the author has found useful in analysis of cardiac *chambers* and vessels and includes the information obtained by fluoroscopy and roentgenograms together.[2]

The study begins with a survey of the thoracic cage, heart, lungs, and diaphragms. Developmental abnormalities of the vertebrae and ribs sometimes occur together with cardiac defects (Fig. 6-66). Patients with cyanotic congenital cardiac lesions, particularly those associated with diminished pulmonary blood flow, are unusually prone to develop *scoliosis* during adolescence. The lower margins of the ribs should be inspected for evidence of notching or scalloping from vessels of collateral circulation in older children or adults with *coarctation of the aorta* (Fig. 6-66) or cyanotic lesions with severe *pulmonary stenosis*.

[2] The following abbreviations are used in Figs. 6-54 to 6-70

A P	—Anteroposterior view	PA	—Pulmonary artery
R A O	—Right anterior oblique view	MPA	—Main pulmonary artery
L A O	—Left anterior oblique view	RPA	—Right pulmonary artery branch
SVC	—Superior vena cava	LPA	—Left pulmonary artery branch
IVC	—Inferior vena cava	Ao	—Aorta
RA	—Right atrium	LAA	—Left aortic arch
RV	—Right ventricle	LDA	—Left descending aorta
LA	—Left atrium	RAA	—Right aortic arch
LV	—Left ventricle	RDA	—Right descending aorta
		C/T	—Cardiothoracic ratio

The diagnoses were proved at postmortem examination in the patients shown in Figs. 6-56, 6-57, 6-59, 6-61, 6-62, 6-64, 6-65, and 6-70C, and at operation, angiocardiography and/or cardiac catheterization in the patients shown in Figs. 6-55, 6-58, 6-63, 6-66, 6-69, 6-70A, and 6-70B.

subvalvular and valvular types; the idiopathic hypertrophic muscular type, however, differs from the others in significant clinical and hemodynamic respects (Braunwald et al). All are characterized by elevation of the left ventricular systolic pressure and by a systolic gradient across the site of obstruction.

Several approaches to the measurement of the gradient across the aortic obstruction are possible Retrograde passage of a catheter from the aorta to the left ventricle permits a pressure tracing to be recorded as the catheter is withdrawn from the ventricle past the obstruction into the aorta, defining the severity of the obstruction and its location with respect to the valve [see Fig 6-53(1)]. An additional advantage of this method is that a selective angiocardiogram can be made with the catheter tip in the left ventricle, providing visualization of the obstruction. This is of particular importance in diagnosing the hypertrophic muscular type.

If the catheter cannot be manipulated retrograde across the aortic valve, the aortic pressure recorded through the catheter can be compared with the left ventricular pressure obtained by direct puncture [Fig 6-53(2)] or by the transseptal route (Ross et al) [Fig. 6-53(1)].

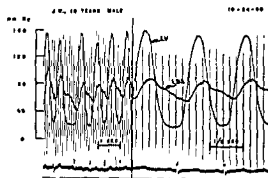


Fig. 6-53(1). Left ventricular pressure obtained by transseptal method compared with brachial artery pressure in a patient with aortic stenosis.

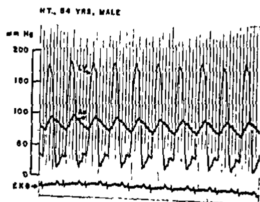


Fig 6-53(2). Left ventricular pressure obtained by direct puncture compared with central aortic pressure in a patient with aortic stenosis

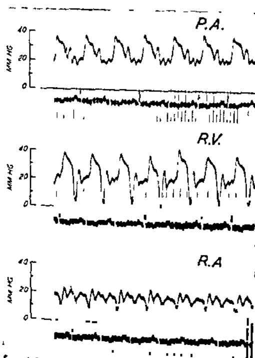


Fig 6-53. Pressure pulses in constrictive pericarditis Characteristic diastolic dips distort the right atrial (RA) and right ventricular (RV) records

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	C/T –Cardiothoracic ratio

The diagnoses were proved at postmortem examination in the patients shown in Figs 6-56, 6-57, 6-59, 6-61, 6-62, 6-64, 6-65, and 6-70C, and at operation, angiocardiography and/or cardiac catheterization in the patients shown in Figs. 6-55, 6-58, 6-63, 6-66, 6-69, 6-70A, and 6-70B

10

Roentgenology in congenital heart disease

MARY ALLEN ENGLE

Of the various radiographic studies that may be performed on patients with heart disease, the two that are the most useful for initial and sequential evaluation are x-rays and fluoroscopy[1] These are carried out in three projections with the patient in the *frontal* and in both the right and the left *anterior oblique positions* while a radiopaque mixture (usually barium) outlines the adjacent structures at the back of the heart. A *lateral* x-ray of the chest may be obtained to supplement the other three views but is less informative than the others and should not be used as a substitute for the oblique projections.

X-rays and fluoroscopy enhance each other in yielding important data on chamber and vessel size, as well as activity *X-rays* have the advantages of causing less radiation to the patient, of showing greater detail of pulmonary parenchymal and vascular markings, and of permanence of the record for immediate as well as subsequent review Fluoroscopy has the advantages of motion for judging the degree and sequence of cardiac pulsations and of flexibility of positioning the patient With the fluoroscope, the heart may be viewed as the patient is rotated, so that each chamber and vessel may be observed to best advantage, thereby providing information that might otherwise be lost if the patient were placed at a set degree of rotation and a film obtained or the fluoroscope turned on. In this manner, unusual contours that are observed can be analyzed as to position, pulsation, and relation to other structures Information gleaned from these radiographic studies forms an integral part of the total evaluation of the patient from the points of view of diagnosis, prognosis, and progress of the patient under medical or surgical management

[1] See Part 3, Chap 8 Editor

GENERAL PRINCIPLES

Technical details of x-ray and fluoroscopy equipment will not be considered here. Suffice it to say that the goal is reproducible clarity of detail of the structures in the thoracic cage and upper abdomen, with minimal radiation of the patient and examiners For x-rays in the pediatric age group, this necessitates appropriate selection of cones and filters to limit radiation of the infant, toddler, or older child. *Whole body irradiation* of the baby undergoing cardiac evaluation is to be condemned, especially when it is realized that several such studies will be done during the lifetime of the patient born with a congenital cardiovascular anomaly With advances in medical and surgical therapy for these conditions, the prospects are now good for a great many to reach adulthood and to have children of their own Protection by appropriate shielding of the lower abdomen and genitalia is desirable. Similar principles apply to fluoroscopy, where irradiation hazard is much greater than with x-rays.

The position of the heart in the chest should be noted. Does it lie in the usual position or more to the left or right than is normal? If it lies more in the left chest than it should, has it been displaced there by some abnormality in the right chest, or is the left lung hypoplastic, the left diaphragm elevated? If the heart lies farther to the right than it should, it may be because of *displacement or dextrorotation*, or there may be a true mirror-image *dextrocardia*. A peek at the ECG is of great benefit before the roentgenographic analysis of a dextrocardia. If it is a mirror-image dextrocardia (indicated on the ECG by inversion of the P and T waves in lead I), then the task of interpretation is simplified, because each view as observed is a mirror-image of the normally placed heart. The right and left anterior obliques can be interchanged and the frontal view mirrored mentally on fluoroscopy or simply turned over if an x-ray. Analysis proceeds as for a levocardia. If the heart is not a mirror image but is dextrorotated, the matter is much more complicated, for the heart may be rotated any amount up to 180°. Landmarks are lost, and one must rely on pulsation to tell which chamber is an atrium, which a ventricle. When dealing with either type of dextrocardia, use of terms "venous" or "pulmonary" and "arterial" or "systemic" atrium and ventricle is recommended instead of "right" or "left," for the latter lead only to helpless confusion in this situation. Sometimes one can use only "anterior" or "posterior" ventricle.

Especially if the heart lies in the right chest, but also for left-sided hearts, it is important to note the position of the diaphragms and the location of the stomach bubble and liver shadow. Occasionally both are on the same side, or there may be complete situs inversus of the abdominal organs (Fig. 6-70B). *Diaphragmatic hernia* is sometimes associated with congenital cardiac anomalies, particularly ventricular septal defect, and *eventration of the diaphragm* is occasionally found together with a hypoplastic lung and pulmonary artery as well as anomalies of pulmonary venous return.

FRONTAL VIEW

Heart Size. An estimate of over-all heart size precedes the more detailed analysis of individual chambers. A simple and reproducible means of estimation is the determination of the *cardiothoracic ratio*. The greatest transverse cardiac diameter (CD) is the sum of *two measurements, from the midline to the* outermost right heart border (MR) and from the midline to the most lateral portion of the left heart border (ML). The cardiac diameter is divided by the thoracic diameter (TD), a measurement of the internal thoracic diameter at the level of the dome of the right diaphragm. The average cardiothoracic ratio is 50 per cent, except for infants, where a figure around 55 per cent is more to be expected. In young children, there may be striking changes in this ratio with variations of inspiration and expiration.

Determination of the cardiothoracic ratio is useful for serial evaluation of heart size, especially in the growing child. To find an average or increased cardiothoracic ratio, however, does not necessarily mean that *the cardiac chambers are normal* in the former or abnormal in the latter situation. For example, there may be marked *hypertrophy of the walls of the right or left ventricle*, yet, if the chamber is *not dilated*, the ratio of heart size to thorax may be in normal limits. Familiar examples of this observation are the "concentric hypertrophy" of the left ventricle in aortic stenosis or of the right ventricle in pulmonic stenosis before dilatation of these chambers has occurred. The boot-shaped heart in tetralogy of Fallot, another example, is characteristically small (Fig. 6-69A, B). Hypertrophy of the muscle wall without increase in internal measurements of that cardiac chamber is often better detected by the ECG than by x-rays or fluoroscopy, but certain changes in contour or pulsations of the ventricle may permit radiographic recognition of ventricular hypertrophy. The enlargement of the heart that is easily detected radiographically, therefore, is usually due to dilatation of cardiac chambers alone or in association with hypertrophy of the walls.

Conversely, an increase in cardiothoracic ratio does not always mean cardiac chamber enlargement. *Intrapericardial fluid* or *mass* may surround a heart of normal size, and overlying extracardiac masses may simulate cardiac enlargement. A frequent point of confusion in infancy, for example, is *thymic enlargement*. A well-penetrated chest x-ray may reveal a normal heart shadow *within the* extracardiac structures, and careful attention to pulsation,



Fig. 6-58. Valvular pulmonic stenosis in a 7-year-old boy. C/T slightly increased. Convex MPA in A P. and R A.O ; branches average; periphery clear. RA quite prominent, RV rounded in frontal view; bulges forward in L.A.O. without much displacement posteriorly of LV. LAA without LA enlargement.

with rudimentary right ventricle (Fig 6-55). They may be increased in amplitude with atrial septal defect (Fig 6-61) and diminished in Ebstein's anomaly of the tricuspid valve (Fig 6-59) or in patients who are in atrial fibrillation.

Sometimes the left atrium becomes so enlarged that it forms part of the right heart border beneath the level of the pulmonary artery (Fig 6-67) In such instances, a *double density* can be seen in the region of the atria, and the barium swallow confirms the enlargement of this posterior atrium When both atria are enlarged, the lower curvature is formed by the right atrium

Analysis of the left heart border in the frontal view, from the top downward, begins with the aorta. The next convexity in the normal heart is the pulmonary artery and the lowermost projection is the left ventricle

Aorta. The first convexity at the left upper cardiac border is the *aortic knob*, formed by the aorta as it arches to the left and becomes the descending aorta (Fig 6-54). The descending portion of the aorta can be traced down as a linear shadow paralleling and to the left of the vertebral column, seen within the density formed by the pulmonary artery and ventricle.

If the expected convexity of the aortic knob is absent, one should seek the explanation in its being obscured, hypoplastic, or abnormally placed The normal aortic knob may be obscured by another more laterally positioned vascular or soft-tissue density, such as a left superior vena cava or the thymus Well-penetrated films will sometimes disclose the aorta within these shadows, and on fluoroscopy, the aortic pulsations can sometimes be detected within the obscuring shadow.

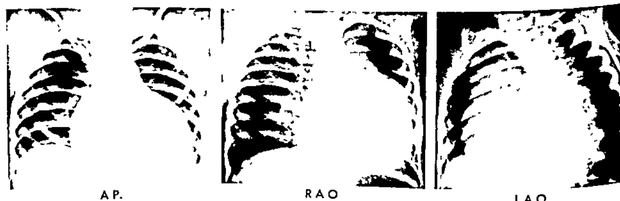


Fig. 6-59. Ebstein's anomaly of tricuspid valve in a 3-year-old boy C/T moderately increased. Concave MPA in A P., R A O ; hypoplastic branches, clear periphery, RA, RV full in A P., R A O, L.A O. and under fluoroscope show damped pulsations L A O , marked displacement posteriorly of LV. R A O shows marked posterior bulge of RA, extends behind the esophagus LAA without LA enlargement.



Fig 6-55. Rudimentary right ventricle with tricuspid atresia, pulmonary stenosis, and atrial septal defect in a 9-month-old boy Small heart. Concave MPA in A P. and R A O.; small RPAs and LPAs, clear lung fields, RA prominent in A P, L A O In L A.O. aorta wide, normally placed; pulmonary window clear



Fig 6-56 Tetralogy of Fallot with infundibular chamber in a 4-year-old girl. Small heart. Concave PA in A P and R A O, small PA branches, clear lung fields Bulge in R A O. in outflow tract of RV is an infundibular chamber. In L A.O, RV bulges forward and the pulmonary window is clear Ao somewhat dextroposed and enlarged, LAA



Fig 6-57. Infundibular pulmonic stenosis in a 10-year-old girl C/T slightly increased Concave MPA, small to average size branches RV full up to MPA in A P, R A O. RA prominent L A O. shows RV bulges, displacing LV, LPA well seen, Ao. not dextroposed. LAA and no LA enlargement with barium swallow



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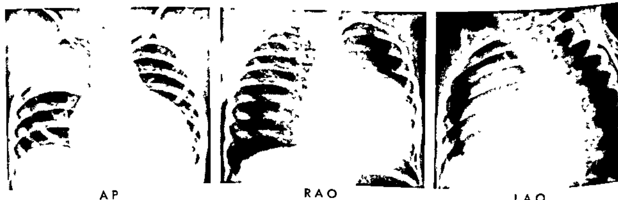


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Fig. 6-56. Tetralogy of Fallot with infundibular chamber in a 4-year-old girl. Small heart. Concave PA in A.P. and R.A.O., small PA branches, clear lung fields. Bulge in R.A.O. in outflow tract of RV is an infundibular chamber. In L.A.O., RV bulges forward and the pulmonary window is clear. Ao somewhat dextroposed and enlarged, LAA.



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Fig. 6-61. Atrial septal defect in a 6-year-old boy. C/T much increased. Large, convex MPA, large branches with wide pulsations. RA enlarged in A.P.; RV enlarged in A.P., R A.O , L A O; LV displaced posteriorly in L A O. Ao. small in A P. and L.A.O. and normal in position LAA without LA enlargement.

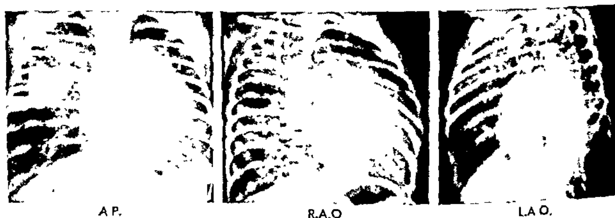


Fig. 6-62. Ventricular septal defect in a 3-month-old girl. C/T moderately increased. Large, *convex MPA in* A.P. and R A O. with huge branches with increased pulsations Ao. small in all *three views and normally placed in* L.A.O *RV full* in A P., R A O , L.A.O, LV full in A P., L A O. LAA with some left atrial enlargement in R A.O.

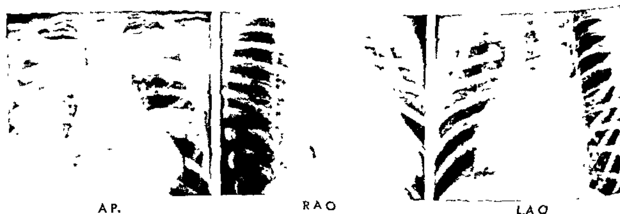


Fig. 6-63. Patent ductus arteriosus in a 7-year-old boy. C/T *slightly* increased. PA convex in A.P., R.A.O. Ao wide in all three views and *in* L.A O., dilated ascending Ao. with wide-amplitude pulsations under fluoroscope LV enlargement *in A.P., L.A O. LA* enlargement. *RV* enlargement in L.A.O. and RA enlargement in A P., somewhat less than enlargement of left heart chambers. LAA.

Hypoplasia of the aorta will cause it to cast a smaller-than-normal shadow. This occurs in some situations in which there is a tremendous left-to-right shunt at the ventricular or atrial level, resulting in a very large main pulmonary artery and a small aorta (Figs 6-61 and 6-62). The aorta is also hypoplastic when there is *atresia of the mitral* or *aortic valves* and the blood supply to the arch of the aorta is provided in retrograde fashion from the pulmonary artery via a patent ductus arteriosus

Displacement of the aorta may occur in several situations

1 The *right aortic arch may persist*, so that the aorta arches to the right, giving off first the innominate artery on the left side and then in turn, on the right side, the right common carotid and the right subclavian artery. The aorta usually descends on the side to which it arches, so that a right descending aorta is to be expected with a right aortic arch (Fig. 6-69A), but the descending aorta may cross behind the esophagus to the opposite side This produces an esophageal anterior displacement that is visualized with a barium swallow

2 The aorta may be normal in size and arch to the left in normal fashion but be pulled out of position by attachment to a fixed structure that retracts it medially This sometimes occurs in *coarctation of the aorta*, where a short ligamentum arteriosum connects the aorta and the pulmonary artery at the level of the coarctation Though the aortic knob may not be visible under these circumstances, the enlarged left subclavian artery may at the same time be brought into view as a convex density that goes straight up or somewhat laterally to the apex of the thorax

3 The aorta may take origin in an abnormal fashion, as in *complete transposition* of the great vessels, where it arises anteriorly and centrally so that it does not cast a shadow at the usual spot for an aortic knob (Fig 6-65) The base of the heart is abnormally narrow in the frontal projection in this condition, but it becomes wider in oblique or lateral views as the vessels are viewed side by side

Now let us consider a different condition, an aorta that is too prominent When the ascending aorta is dilated, it forms part of the right heart border just superior to the right branch of the pulmonary artery (Figs 6-63, 6-64, and 6-66) The aorta then sweeps

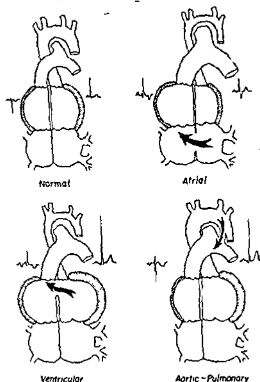


Fig. 6-60. Differential diagnosis of sites of left-to-right shunts

over to the left to make a large aortic knob as it becomes the descending aorta The causes for such dilatation are numerous, e.g , when the aorta is the great vessel that receives most of the cardiac output, as in a tetralogy with pulmonary atresia or extreme stenosis, or in a true truncus arteriosus (Fig 6-64). The ascending aorta is dilated when there is an aortic septal defect or large patent ductus arteriosus (Fig. 6-63), both conditions of increased pulmonary arterial, left heart, and aortic blood flow. The aorta is dilated distal in aortic valvular disease, either stenosis (Fig. 6-67) or insufficiency. In the former, the pulsations appear damped and in the latter, bounding Disease of the aortic wall is another cause of dilatation, as in aortitis, medial *necrosis, or aneurysm*

Pulmonary Artery. The next area downward along the left heart border is normally a convexity *formed by the main pulmonary artery* after it leaves the outflow tract of the right ventricle and before it divides into the *left and right stems* (Fig 6-54). The left stem dips behind the main pulmonary artery and then extends into the left lung as a comma-shaped structure of diminishing size as it branches

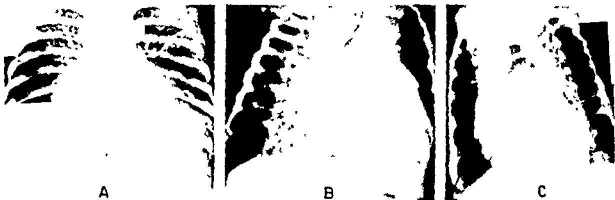


Fig. 6-67. Valvular aortic stenosis in an 8-month-old boy. C/T much increased. Pulmonary vascularity average. Dilatation of ascending Ao. in L.A.O. (C). Marked enlargement of LV in A. P. (A), LA O. (C). Marked enlargement of LA in R.A.O. (B). LA is border forming in A P.; note high rounding due to enlargement of LA in contrast to low rounding due to enlarged RA (cf. Fig. 6-61). RV questionably slightly enlarged or displaced forward in L.A O. (C), R A O (B). LAA.

peripherally Much of the right pulmonary stem is hidden behind the heart, but when it emerges in the right hilus, it resembles the left branch as it curves downward and vessels fan out from it Normally, pulsations of small amplitude are visible in the main pulmonary artery and the medial portions of the right and left stems Deviations from the normal are in the form of diminished or exaggerated convexity and pulsation of these vessels

Concavity in the region of the main pulmonary artery means that the vessel is atretic, hypoplastic, or misplaced In the first two situations, the lung fields contain fewer blood vessels than is normal and therefore appear unusually "clear" or radiolucent The pulmonary artery may be *atretic* at its origin, and both stems may be absent, in which case there is a concavity in the region of the main pulmonary artery and no hilar "commas" Instead, there is a fine, lacy, stippled appearance in the hilar regions due to vessels of collateral circulation. Even though there is atresia of the pulmonary artery at its origin, one or both stems may be patent distally, so that a small vessel can be seen in the position of the right or left stem of the pulmonary artery. The heart may be displaced toward the side of an absent pulmonary artery, and the ipsilateral lung may be underdeveloped It is particularly important to determine the presence or absence of the pulmonary artery on each side if an anastomosis (subclavian-pulmonary or aortopulmonary anastomosis) is contemplated.

More often, when this segment is concave, it is because the main pulmonary artery is *hypoplastic* This is usually due to *infundibular pulmonic stenosis*, most often in association with a ventricular septal defect and large aorta, as in the tetralogy of Fallot (Figs 6-56 and 6-69B) Rarely, the infundibular stenosis is an isolated anomaly (Fig 6-57) The small size



Fig. 6-68. Double aortic arch with right descending aorta in a 3-month-old girl. C/T average. Pulmonary blood flow average In A.P., barium column indented and constricted on both the right and left sides by LAA and by RAA Barium descends to left of midline, where it is displaced by RDA. R.A.O. and L.A.O: Esophagus constricted and pushed forward by large vessel the size of an aorta just below region of aortic arch.

Hypoplasia of the aorta will cause it to cast a smaller-than-normal shadow. This occurs in some situations in which there is a tremendous left-to-right shunt at the ventricular or atrial level, resulting in a very large main pulmonary artery and a small aorta (Figs 6-61 and 6-62). The aorta is also hypoplastic when there is *atresia of the mitral* or *aortic valves* and the blood supply to the arch of the aorta is provided in retrograde fashion from the pulmonary artery via a patent ductus arteriosus

Displacement of the aorta may occur in several situations:

1. The *right aortic arch may persist*, so that the aorta arches to the right, giving off first the innominate artery on the left side and then in turn, on the right side, the right common carotid and the right subclavian artery The aorta usually descends on the side to which it arches, so that a right descending aorta is to be expected with a right aortic arch (Fig 6-69A), but the descending aorta may cross behind the esophagus to the opposite side This produces an esophageal anterior displacement that is visualized with a barium swallow

2 The aorta may be normal in size and arch to the left in normal fashion but be pulled out of position by attachment to a fixed structure that retracts it medially This sometimes occurs in *coarctation of the aorta*, where a short ligamentum arteriosum connects the aorta and the pulmonary artery at the level of the coarctation. Though the aortic knob may not be visible under these circumstances, the enlarged left subclavian artery may at the same time be brought into view as a convex density that goes straight up or somewhat laterally to the apex of the thorax

3 The aorta may take origin in an abnormal fashion, as in *complete transposition* of the great vessels, where it arises anteriorly and centrally so that it does not cast a shadow at the usual spot for an aortic knob (Fig 6-65) The base of the heart is abnormally narrow in the frontal projection in this condition, but it becomes wider in oblique or lateral views as the vessels are viewed side by side

Now let us consider a different condition an aorta that is too prominent When the ascending aorta is dilated, it forms part of the right heart border just superior to the right branch of the pulmonary artery (Figs. 6-63, 6-64, and 6-66) The aorta then sweeps

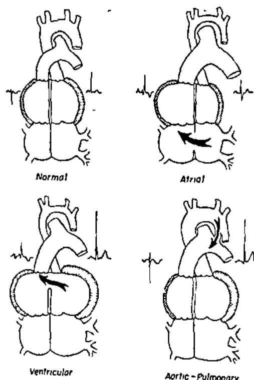


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the lung fields should be inspected by x-ray and fluoroscopy for evidences of other vascular anomalies. A pulsating density, of a size out of proportion to the normal vessels in that segment of lung, suggests an *arteriovenous fistula*. A vascular shadow that does not follow the normal fanning-out pattern of the branching arterial tree suggests an *anomalously draining pulmonary vein*. Multiple thin transverse lines at the lung bases are found in some patients with pulmonary venous congestion and are thought to represent *prominent lymphatic channels*. A peculiar, evenly stippled appearance to the lung fields is observed in some patients with infradiaphragmatic total anomalous pulmonary venous drainage. Presumably this pattern is due to *pulmonary venous obstruction*. A similar picture may be observed in pulmonary hemosiderosis.

Though the arterial supply and venous drainage of the lungs are usually bilaterally symmetrical, the two sides may be quite different. For example, one side may be devoid of a pulmonary artery and the other lung normally filled or flooded Vessels of collateral circulation to the lungs may be better developed on one side than the other. Therefore, the two lung fields should be inspected individually and compared with each other, as well as with the mental image of the normal pulmonary vascular bed.

Left Ventricle. In the normal person, the next and lowermost bulge on the left heart border represents the left ventricle. But, under certain circumstances of left atrial or right ventricular enlargement, an additional convexity is interposed: the *left auricular appendage* or the *outflow tract of the right ventricle*. It can be decided which of these chambers is responsible for the enlargement by noting the timing and character of pulsations to determine whether they are atrial or ventricular and by seeking other evidences of enlargement of these chambers: deviation of the barium-filled esophagus by an enlarged left atrium and fullness of the outflow tract of the right ventricle in the RAO projection.

The apex of the heart is usually formed by the left ventricle. If the apex extends too far laterally, there may be enlargement of one or both of the ventricles. Oblique projections are often more helpful in telling which ventricle,



Fig. 6-69. A. Right aortic arch and right descending aorta in a 19-year-old boy. Aortic knob absent on left but visible on right within shadow of SVC which it displaces laterally. Barium column curves to left around the RAA and descends to left of midline, displaced there by RDA Small heart with RV enlargement, slightly convex MPA, hypoplastic right and left branches and clear lung fields Patient has tetralogy of Fallot with valvular pulmonic stenosis. B. Retroesophageal right subclavian artery in a 9-year-old girl. Barium swallow reveals oblique filling defect from below on left side upward to right side Barium curves to right around the LAA and descends in midline adjacent to LDA Aortic knob and descending aorta well seen on left side. Small boot-shaped heart with RV enlargement, concave MPA segment, and clear lung fields in patient with tetralogy of Fallot C Retroesophageal vessel of collateral circulation to the lungs in a 3-month-old boy. Note sharp incurving of esophagus about level of pulmonary arteries This is due to a vessel of collateral circulation arising from the descending aorta and coursing behind the esophagus to anastomose with pulmonary arteries in the lung fields A continuous murmur over the lung fields posteriorly was produced during life by this vessel. Infant with tetralogy of Fallot and pulmonary atresia (pseudotruncus arteriosus).



Fig 6-64. Common truncus arteriosus in a 6-month-old girl C/T markedly increased. MPA region concave in A P, R A O; yet large PA branches with increased pulsations. "Aorta" wide in all three views. LV greatly enlarged in A P. and L.A O RV also enlarged, but less than LV, in L A O, R A O. LA forms a double density in A P. Esophagram (not shown in these pictures) confirmed LA enlargement.



Fig. 6-65. Complete transposition of the great vessels in a 1-month-old boy. C/T *much increased* MPA region concave in A P and R A O, yet large PA branches and increased pulmonary vascular markings throughout Base of heart narrow in A P. and twice as wide in R A O. and L A O LV enlargement (A P. and L A O.) and RV enlargement (A.P., L A.O, R A.O.) Atria less enlarged Barium swallow not reproduced well, slight LA enlargement.



Fig 6-66 Coarctation of *aorta* in an 18-year-old boy C/T *average* Pulmonary blood flow average. MPA obscured within shadow of dilated descending Ao Convexity of aortic knob above that of poststenotic segment of descending Ao Dilated *ascending Ao* in A P. Barium swallow in R.A O. and *left lateral* shows anterior displacement of *esophagus by* poststenotic dilatation of descending Ao No LA enlargement LAA Scalloping of undersurface of ribs bilaterally. Congenital anomaly of rib cage on left.

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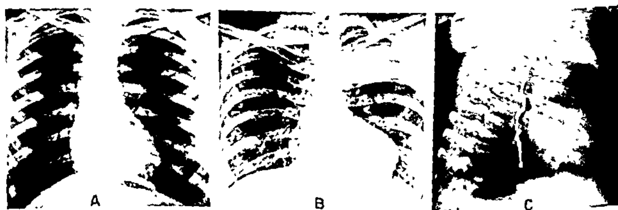


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of the pulmonary artery is evident in the stems as well. Under the fluoroscope, pulsations are diminished to absent in these vessels.

Displacement of the pulmonary artery as a cause of concavity in that region comes about either through rotation of the heart or through malposition of the vessel itself. Examples of rotational changes are the varying degrees of congenital dextrorotation of the heart, as well as great enlargement of the left ventricle, so that the pulmonary artery is rotated out of view. In either event, where rotation is a factor, the convex pulmonary artery can usually be located when the patient is turned into the oblique projections.

Actual *malplacement of the pulmonary artery* with resultant concavity of the pulmonary artery segment occurs chiefly in the following two conditions. (1) When there is *complete transposition* of the great vessels (Fig. 6-65), the pulmonary artery arises from the left ventricle as the posterior great vessel, and in "corrected" transposition complexes, the pulmonary artery arises posteriorly and medially. (2) When there is a *common truncus arteriosus* (Fig. 6-64), the pulmonary stems arise from the common trunk, usually at a distance from the outflow tract of the ventricle. In *transposition* complexes, as well as in true truncus arteriosus, the pulmonary blood flow is unobstructed and is greater than normal, so that the lung fields appear "plethoric" and under the fluoroscope the pulmonary artery branches may exhibit increased pulsations. In an infant with congenital heart disease the combination of concave pulmonary artery segment and flooded lung fields should suggest a transposition of the great vessels or truncus arteriosus. In the former, the base of the heart appears narrow in the frontal view, where the two vessels lie one in front of the other, but the base broadens in the oblique projections as the vessels are seen side by side. In the latter, the base of the heart is equally wide in all views when there is a single large truncus.

Unusual convexity of the pulmonary artery is due to dilatation of that vessel, which can occur for several reasons. (1) *Dilatation is distal* to valvular pulmonic stenosis (Fig. 6-58) or *proximal* to peripheral pulmonary artery stenoses or pulmonary venous obstruction. (2) The dilatation may be due *to increased volume* of pulmonary blood flow associated with a large arteriovenous shunt at the atrial, ventricular, or aortopulmonary levels (Figs. 6-60 to 6-63). (3) There is a rare situation, designated *idiopathic dilatation of the pulmonary artery*, where no functional abnormalities can be detected to account for the large size of the pulmonary artery. The dilatation in any of these situations may assume aneurysmal proportions.

Pulmonary Vascular Bed. The nature of the pulmonary vasculature beyond the dilated vessel serves to differentiate the causes of the dilatation. When there is *valvular pulmonic stenosis* (Fig. 6-58), the right and left stems decrease quickly in size and the peripheral pulmonary vasculature is clearer than usual, especially if there is a right-to-left shunt, so that the pulmonary circulation is actually depleted. Though pulsations may be seen in the main pulmonary artery, where the jet of blood coming through the stenosed valve strikes the wall and swirls about, the pulsations in the stems are reduced or absent.

If the obstruction is distal to the valve and *is in the peripheral pulmonary arteries or arterioles*, the pulmonary stems or branches are enlarged out to the region of obstruction, around the middle third of the lung field (going from hilus to periphery), then stop abruptly and the peripheral lung fields are excessively clear. If the obstruction is distal to the pulmonary arterioles, the pulmonary arteries are enlarged throughout and taper gradually. In addition, there may be a hazy appearance to the lung fields due to pulmonary venous distention. Pulsations in the main pulmonary artery and its branches may be more vigorous than normal but are less prominent than those seen in enlarged pulmonary arteries when there is a left-to-right shunt.

In lesions where the volume of pulmonary blood flow greatly exceeds the systemic flow, the main pulmonary artery and branches are engorged and overactive. In the hilar areas, round densities representing pulmonary artery branches seen end on are found (Figs. 6-61 to 6-63 and 6-70C). Pulsations in the pulmonary arteries are exaggerated, especially if the malformation is an atrial or ventricular septal defect. The *hilar dance* in patients with patency of the ductus arteriosus is usually less marked than with septal defects.

While viewing the pulmonary arterial tree,

developed right ventricle, the entire anterior aspect of the heart in this view is formed by the right atrium (Fig 6-55), which can be seen to pulsate before the posteriorly placed left ventricle. The right atrium may pulsate more vigorously than normal in patients with tricuspid atresia, but in Ebstein's anomaly of the tricuspid valve (Fig. 6-59) (another example where the right atrium can form the anterior cardiac border in the LAO projection), the pulsations are quite damped When the tricuspid leaflets are plastered down against the right ventricular wall, so that their free margins divide that chamber into a distal portion that functions as a right ventricle and a proximal chamber that is atrialized, the proximal portion becomes dilated and exceedingly thin-walled Its pulsations may be barely perceptible and are in contrast to the normal pulsations of the left ventricle behind

Right ventricular pulsations are often increased in vigor or amplitude in those conditions causing enlargement of that ventricle. When the right ventricle enlarges, it bulges not only forward but backward as well, displacing the left ventricle posteriorly (Figs 6-57, 6-59, and 6-61). It may then be very difficult to decide about the size of the left ventricle whether it is also enlarged or is merely pushed back. If the patient can take a deep enough breath so that the interventricular groove on the bottom of the heart can be visualized, this question can be answered The groove marks the separation between anterior and posterior ventricle. It should be at the mid-point between anterior and posterior heart border if the ventricles are of equal size, but is displaced posteriorly by enlargement of the right ventricle. Unfortunately, in patients with much ventricular enlargement, the ventricles cover so much of the diaphragmatic surface that the groove cannot be seen, either with a deep breath or with the stomach filled with carbonated beverages for better contrast Radiographically, to determine left ventricular enlargement in the presence of much right ventricular enlargement, one must sometimes rely on collateral evidence of left-sided involvement. For example, the presence of left atrial enlargement or aortic abnormality would be in favor of left ventricular enlargement.

The posterior aspect of the heart shadow in the LAO projection is formed by the aortic arch above, the pulmonary stems just below that, then the left atrium, and the bulk of the shadow by the left ventricle.

The transverse arch and descending aorta in this view have been alluded to. *Coarctation of the aorta* with poststenotic dilatation (Fig 6-66), *aneurysms* in this region, and the absence of the descending aorta on the left because *it descends on the right* are the chief abnormalities to be reckoned with

Deviations in the pulmonary stems and branches, which normally fill the aortic window, are next in line for analysis. Diminutive size of the pulmonary stems produces an unusually clear window, especially if the aorta is at the same time dextroposed, as in *tetralogy of Fallot* (Fig. 6-56). Large and abnormally pulsating pulmonary arteries are also well seen in this view (Fig. 6-62).

The left atrium lies just beneath the bifurcation of the bronchi and atop the left ventricle. Unless it enlarges considerably, so that it displaces the left main bronchus upward, the left atrium is not well seen in this view Fortunately, however, the esophagus hugs the posterior wall of the left atrium and can be filled with contrast medium, so that changes in size of that chamber can more readily be perceived This will be discussed later under the heading Esophagram.

The major portion of the posterior cardiac border in the LAO projection is formed by the left ventricle Its relationship to the vertebral column forms a convenient way of estimating left ventricular or cardiac size In the normal person with quiet respirations, the posterior border of the heart (the left ventricle) clears the anterior border of the vertebrae at 50° of rotation. Increase in this angle of clearance is due to left ventricular enlargement or displacement or to extracardiac fluid or mass

RIGHT ANTERIOR OBLIQUE POSITION

The patient is turned into the RAO position, so that his right shoulder is next to the fluoroscopic screen and the heart no longer overlaps the spine The right ventricle, its outflow tract, and the main pulmonary artery are in silhouette anteriorly, with the aorta at the top. The left atrium forms the posterior heart border.

but in the frontal view there are certain clues that point to one or the other. If the apex extends outward and downward toward the diaphragm, the left ventricle is suspect (Figs. 6-63 and 6-64). But if the apex is tipped outward and upward, so that it points away from the diaphragm (Figs. 6-56 and 6-69B) or if the rounding of the apex begins high beneath the pulmonary artery (Figs 6-57 to 6-59 and 6-61), this is probably due to enlargement of the right ventricle, which has displaced the left ventricle outward and upward or which has enlarged to such an extent that it forms the apex of the heart Enlargement of both ventricles produces a combination of these findings: the ventricular shadow bulges downward, outward, and upward, but marked enlargement of either ventricle alone can duplicate these changes (Fig 6-61) At this stage, rotation of the patient into the LAO projection helps Here, the right ventricle comes forward and the left ventricle forms the posterior heart border, and each can be seen to better advantage.

LEFT ANTERIOR OBLIQUE POSITION

Nomenclature has been standardized for the oblique views, so that the cardiac chambers are viewed in the same projection, regardless of whether the fluoroscope screen is next to the patient's left side (as it is in the LAO view) or the x-ray cassette is against his right side.

In this projection, the uppermost shadow is formed anteriorly by the *aorta* as it ascends. It arcs posteriorly and becomes more difficult to visualize as it descends because it is superimposed on the vertebral column This projection is an excellent one for determining dilatation of the ascending aorta (Figs. 6-63 and 6-67), transposition (Fig. 6-65), or marked dextroposition of the aorta (Fig 6-56). When the aorta arises abnormally far forward, it must make a wider sweep in the transverse portion before it descends Thus there is a *wide aortic window*, that area between the posterior aspect of the ascending aorta and the anterior portion of the descending aorta

The right atrium (above) and the right ventricle (below) form the anterior aspect of the heart in the LAO projection. Enlargement of either or both of these chambers will cause a forward bulge of the cardiac shadow (Figs 6-55 to 6-59 and 6-61). Fluoroscopic timing of pulsations will tell whether atrium or ventricle is responsible for the enlargement.

In instances of *tricuspid atresia* with under-

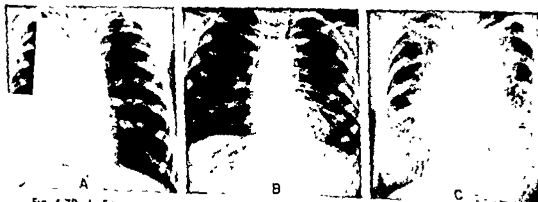


Fig 6-70 A Situs inversus with dextrocardia in an 8-year-old boy Small heart with apex on right, stomach bubble on right Note bilateral SVC, concave MPA segment on right, average-sized PA branches, and convexity in region of outflow tract of ventricle The latter is a rudimentary outlet chamber in this patient who has a single ventricle and slight pulmonic stenosis B Situs inversus with levocardia in a 5-year-old girl. C/T not increased Apex on left Stomach bubble on right Liver on left Straight shadows on right and left at base of heart represent bilateral SVC Concave MPA Slightly decreased pulmonary vascularity C. Total anomalous pulmonary venous return to left superior vena cava in a 42-year-old woman C/T increased Pulmonary blood flow much increased RA enlargement and RV enlargement Great vascular collar encircles base of heart because of drainage of all pulmonary veins into left superior vena cava (or left innominate vein), which is greatly dilated, as is superior vena cava on right, which receives this admixed blood and leads it into RA, RV, and PAs Small atrial septal defect was only entry of blood into left side of heart and systemic circulation.

When *coarctation of the aorta* occurs at the usual place below the left subclavian artery, and there is poststenotic dilatation of the descending aorta, this dilated area acts as a retroesophageal vessel and bows the barium column forward in the LAO projection (Fig. 6-66). If intercostal arteries become much enlarged in patients with *coarctation*, these too are small retroesophageal vessels which can be identified on barium swallow.

Sometimes, in patients with great enlargement of the pulmonary artery and its main stems, there can be seen in the LAO projection a forward displacement of the esophagus at the level of the pulmonary artery branch.

Equal attention is paid to the esophagus, where it is in contact with the left atrium. In acquired heart disease, *this is the chief* point of interest in the esophagram because of the information to be obtained about the size of the left atrium One should not rely on a single view to determine the presence or absence of left atrial enlargement, because different degrees of enlargement may affect the esophagus in various ways, so that even gross enlargement may be missed if the barium swallow is done in only one view. One may gain a false impression of left atrial enlargement if the esophagus is not completely filled or if the diaphragms are elevated. In this respect, fluoroscopy has an advantage over films in eliminating these artefacts.

The single most useful view for detecting the various degrees of *left atrial* enlargement is the RAO projection, where the esophagus is deviated posteriorly in a greater or lesser curvature, depending on the degree of enlargement (Figs 6-62, 6-63, and 6-67)

At the same time that the esophagus bows posteriorly in the RAO projection, it curves to the right and then swings back to the midline in the frontal view

If the esophagus has been displaced, as described in the above two views, it usually falls undisturbed in the LAO projection

Occasionally, however, the esophagus swings to the left of the midline in the frontal projection, curves posteriorly in the LAO projection, and falls straight in the RAO view This is particularly true if the left atrium is markedly enlarged

In the lateral view, the esophagus swings posteriorly if it is displaced by a large left atrium, but may not be deviated at all in slight degrees of enlargement, and with some enlargement the barium column may be displaced more in one or the other of the obliques than in the lateral view.

Therefore, to evaluate the size of the left atrium by its effect on the adjacent esophagus, it is important to visualize the esophagus in multiple projections.

INTERPRETATION OF RESULTS

When the various pieces of information have been gleaned from a careful perusal of the x-rays and fluoroscopy of the heart and lungs in the frontal and both oblique projections, they must be assembled for a working diagnosis of the patient's heart condition. The final clinical *impression* should be a synthesis of all pertinent information—the history, physical findings, ECG, and indicated special procedures as well as *radiologic* studies. No single piece of information should be assigned diagnostic significance out of context with other available data. Each part of the diagnostic work-up has much to offer, and when all parts are considered together, a sound diagnosis can usually be reached

It is important that some clinical information be available at the time of analysis of radiographic studies because a different interpretation may be in order if it is known that the patient is *cyanotic*, for example, rather than of normal color. And the findings will be interpreted with greater caution if it is known that the patient is *in heart failure* than if it is assumed that the abnormalities observed are the usual condition for that patient If the patient has an acute febrile illness suggesting *pneumonia*, interpretation of the markings in the lung fields might be more in favor of bronchopneumonia than of increased pulmonary blood flow or congestive heart failure, conditions that would be suggested in a patient without a history of respiratory infection. Incidentally, the precise recognition of superimposed bronchopneumonia or left-sided heart failure in an infant or child with greatly increased pulmonary blood flow is fraught with difficulty.

With these reservations then, let us consider how a *radiologic diagnosis* is reached The most difficult conditions to diagnose are in those patients with congenital heart disease

The normal right ventricle curves gently upward, then gives off a normally convex main pulmonary artery (Fig. 6-54). Right ventricular enlargement exaggerates this curve (Figs. 6-56 to 6-59 and 6-61) The ventricle may extend to the chest wall and even be flattened against it for several centimeters. It should be noted that marked left ventricular enlargement can be solely responsible for an extension of the cardiac silhouette forward and downward in this view, thus suggesting associated right ventricular enlargement. This problem in differential diagnosis of ventricular enlargement may be resolved by finding associated signs of right-sided cardiac enlargement, e.g., evidence of enlargement of the pulmonary artery or of the right atrium, which would favor the presence of right ventricular enlargement The ECG may also help.

If there is *infundibular pulmonic stenosis*, the outflow tract of the right ventricle has a scooped-out concave appearance in this and the frontal view (Fig 6-57) The RAO position is excellent for detecting an infundibular chamber distal to infundibular narrowing. The chamber can be identified as a separate bulge in the outflow portion of the ventricle proximal to the region of the main pulmonary artery (Fig 6-56) A rudimentary outlet chamber in a patient with a single ventricle has a similar appearance (Fig 6-70A)

The main pulmonary artery, as it springs from the right ventricle, is seen to best advantage in the RAO projection Unusual concavity or convexity has the same significance as described in the frontal projection Occasionally, the main pulmonary artery may be more centrally placed than is usual, so that the pulmonary artery segment in the frontal view is concave Careful search as the patient is rotated into the RAO projection may reveal it as a normally convex structure

The left atrium forms the posterior cardiac border Behind it lies the esophagus This is the most sensitive position for detecting slight, as well as gross, degrees of left atrial enlargement by the posterior swing of the barium-filled esophagus around the left atrium

Occasionally, the right atrium may be so enlarged that it projects far backward, overlapping the left atrium and forming the posterior margin of the heart (Fig 6-59) Barium swallow serves to differentiate right from left atrial enlargement under these circumstances: if there is no displacement of the barium-filled esophagus in this or other views, it is the right atrium, not the left, that is responsible for the posterior curve

LATERAL VIEW

This is the least valuable of the four positions for discrete analysis of cardiac chambers and vessels One can sometimes gain the impression that the heart is enlarged more anteriorly than posteriorly and that the retrosternal space has been encroached upon more than is normal, but other projections are needed for confirmation. Marked degrees of left atrial enlargement may produce more deviation of the barium-filled esophagus in this view than in the others.

ESOPHAGRAM

When a patient is being fluoroscoped, a swallow of thick contrast material (usually barium) to outline the esophagus, as the patient is rotated through the three views, completes the study For chest x-rays also, the esophagus should be filled with barium in all three views This necessitates three swallows of the chalky mixture Therefore, especially for children, the few minutes required to flavor the mixture for palatability and to make it thick enough so that it does not disappear before the picture is taken represent time well spent.

In the frontal view, the esophagus curves to the right at the level of the aorta which arches to the left and then descends straight down the midline behind the left atrium and to the right of the descending aorta to pass through the diaphragm and into the stomach on the left (Fig 6-54).

When dealing with patients with congenital cardiac anomalies, it is well to maintain an interest in the course of the barium until it is in the stomach, for in this way one can identify some developmental anomalies of the gastrointestinal tract as well: complete or partial situs inversus of the abdominal organs in patients with levocardia (Fig 6-70B) or dextrocardia (Fig 6-70A). Often these anomalies are suspected before the barium swallow, but it usually comes as quite a surprise to find, in a patient where the liver has been palpated or percussed in the right upper quadrant, that

When *coarctation of the aorta* occurs at the usual place below the left subclavian artery, and there is poststenotic dilatation of the *descending aorta*, this dilated area acts as a retroesophageal vessel and bows the barium column forward in the LAO projection (Fig. 6-66). If intercostal *arteries become much enlarged in patients* with coarctation, these too are small retroesophageal vessels which can be identified on barium swallow.

Sometimes, in patients with great enlargement of the pulmonary artery and its main stems, there can be seen in the LAO projection a forward displacement of the esophagus at the level of the pulmonary artery branch

Equal attention is paid to the esophagus, where it is in contact with the left atrium. In acquired heart disease, this is the chief point of *interest in the esophagram* because of the information to be obtained about the size of the left atrium One should not rely on a single view to determine the presence or absence *of left atrial enlargement*, because different degrees of enlargement may affect the esophagus in various ways, so that even gross enlargement may be missed if the barium swallow *is done in only one view*. One may gain a false impression of left atrial enlargement if the esophagus is not completely filled or if the diaphragms are elevated In this respect, fluoroscopy has an advantage over films in eliminating these artefacts

The single most useful view for detecting *the various degrees of left atrial enlargement* is the RAO projection, where the esophagus is deviated posteriorly in a greater or lesser curvature, depending *on the degree* of enlargement (Figs. 6-62, 6-63, *and* 6-67)

At the same time that the esophagus bows posteriorly in the RAO projection, it curves *to the right* and then swings back to the midline in the frontal view

If the esophagus has been displaced, as *described in* the above two views, it usually falls undisturbed *in the LAO projection*

Occasionally, however, the esophagus swings to the left of the midline *in the frontal projection*, curves posteriorly in the LAO projection, and falls *straight in the RAO* view This is particularly true if the left atrium is *markedly* enlarged

In the lateral view, *the esophagus* swings posteriorly if it is displaced by a large left atrium, but may *not* be *deviated* at all in *slight* degrees of enlargement, and with some enlargement the barium column may be displaced *more* in one or the other of the obliques than in the lateral view.

Therefore, *to* evaluate the size of the left atrium by its effect on the adjacent esophagus, it is important to visualize the esophagus in *multiple* projections.

INTERPRETATION OF RESULTS

When the various pieces of information have been gleaned from a careful perusal of the x-rays and *fluoroscopy of the* heart and lungs in the frontal and both oblique projections, they must be assembled for a working diagnosis of the *patient's heart condition*. The final clinical impression should be *a synthesis* of all pertinent information—the history, physical findings, ECG, and indicated *special* procedures as well as radiologic studies. No single piece of information should be assigned diagnostic significance out of context with other available data. Each part of the diagnostic work-up has much to offer, and when all parts are considered together, a sound diagnosis can usually be reached

It is important that some clinical information be available at the time of analysis of radiographic studies because a different interpretation may be in order *if it is known that* the patient is *cyanotic*, for example, rather than of normal color. And the findings will be interpreted with *greater caution* if it is known that the patient is in *heart failure than if it* is assumed that the abnormalities observed are the usual condition for that patient. If the *patient has an* acute febrile illness suggesting *pneumonia*, interpretation of the *markings in* the lung fields might be more in favor of bronchopneumonia than of increased pulmo*nary blood flow* or congestive heart failure, conditions that would be suggested in a patient without a history of *respiratory* infection. *Incidentally*, the precise recognition of super*imposed bronchopneumonia* or left-sided heart failure in an infant or child with greatly increased pulmonary blood flow *is* fraught with difficulty.

With these reservations *then, let us* consider how *a radiologic diagnosis* is *reached*. *The most* difficult conditions to diagnose are *in those patients with* congenital heart disease

the barium curves to the right below the diaphragm to enter a stomach that is also in the right upper quadrant.

In the LAO projection, the barium mixture falls straight down, without indentation by structures in front or behind (Fig. 6-51).

In the RAO view, the barium column curves posteriorly about the left aortic arch and then hugs the back of the heart as it descends in a straight line, without indentation, toward the stomach (Fig. 6-51). In infancy, the aorta as it arches may impinge very little on the esophagus. One then identifies the left aortic arch because there is evidence of a left descending aorta and no retroesophageal vessels.

The structures which cause any departure from the above course of the esophagus are the aorta, or some of its branches, and the left atrium. Neither the right atrium nor right or left ventricle is in contact with the esophagus and, therefore, cannot alter the esophagram.

One of the common aortic anomalies is a *right aortic arch* and *descending aorta* This can occur as an isolated abnormality or in association with other cardiac anomalies It is found in about 25 per cent of patients with a tetralogy of Fallot. Persistence of the right aortic arch gives a mirror image of the normal course of the aorta and a mirror image of the normal esophagram In frontal view, the barium curves to the left at the level of the right aortic arch, and it descends to the left of the midline, where it is displaced by the *right descending aorta* (Fig 6-69A) In the LAO projection, the barium curves posteriorly at the level of the arch, and in the RAO view, it falls freely without indentation Rarely does the aorta pass behind the esophagus before arching to the right.

Sometimes the aorta arches to one side, then crosses over high in the thorax and descends on the opposite side If it does so, the side of the arch is identified by the direction it displaces the esophagus in the frontal and oblique projections, as described above Then the esophagus kinks abruptly or obliquely in the frontal view as the aorta crosses behind it, and in the oblique projections, the esophagus curves forward around the retroesophageal aorta The side on which the aorta descends is identified in the frontal view by whether the barium descends in the midline (left descending aorta) or to the left of the midline. One can also visualize the descending aorta if the patient is turned into the oblique projection corresponding to the side on which the aorta descends, e g, RAO for right-sided descending aorta.

Here is an illustration of such an analysis· if the barium curves to the right in the frontal and RAO views, there is a left aortic arch A large forward bowing of the esophagus just below the level of the aortic arch indicates a retroesophageal course of the aorta, and the descent of the barium column in frontal view to the left of the midline confirms the fact that the aorta has crossed over to descend on the right side (Fig. 6-68).

A similar analysis holds for patients with a *vascular ring* and a *double aortic arch* (Fig 6-68). Each component is identified by the manner in which it affects the esophagus However, if one part of the ring is hypoplastic or a ligament, then the presence of only the well-developed arch and a retroesophageal vessel will be manifest.

Other aortic arch anomalies recognizable by changes in the esophagram produce a forward displacement of the esophagus in one or both oblique views because of their retroesophageal location. These include *aberrant right subclavian artery* (Fig 6-69B), *anomalous vessels* of collateral circulation from aorta to lungs (Fig. 6-69C), and *coarctation of the aorta* (Fig. 6-66)

Aberrant right subclavian artery comes off below the left subclavian artery as the last of the brachiocephalic vessels, and it crosses behind the esophagus and obliquely upward to enter the right arm Thus in the oblique projections the esophagus is pushed forward, and in the frontal view there is an *oblique filling defect*, low on the left and high on the right side (Fig. 6-69B) Aberrant subclavian artery has been associated with *dysphagia lusoria*, but in the pediatric age group symptoms are rare.

Anomalous vessels from the aorta to the lungs alter the barium swallow when they come off the descending aorta and pass behind the esophagus to anastomose with the pulmonary arteries These collaterals may be single or multiple, and if of sufficient size, they indent the esophagus on its posterior aspect and can be identified in oblique or lateral views (Fig. 6-69C).

amount of blood. The systemic venous return plus the large volume of *arterial blood travel* through the right atrium, ventricle, and pulmonary artery, all of which are dilated. The left ventricle and aorta, by contrast, receive a *smaller amount of blood and are not enlarged.* Compared to the pulmonary artery, the aorta is the smaller vessel and may be normal in size or hypoplastic. *Unless there is obstruction* to outflow from the right ventricle (pulmonary stenosis or increased pulmonary vascular resistance), *there is not much hypertrophy* of the wall of the right ventricle.

If the shunt occurs distal to the AV valves, the augmented pulmonary blood flow is returned to the left atrium and the left ventricle before partitioning, so *left ventricular enlargement* (dilatation and hypertrophy) appears. If the shunt is *at the ventricular level,* then part of this blood enters the right ventricle and pulmonary artery, which are dilated. The remainder enters the aorta in normal or subnormal amount, so that the aorta is actually or relatively small in comparison with the pulmonary artery.

If the shunt is at the *aortopulmonary level,* the large amount of blood *returning from the* lungs passes through the left atrium, left ventricle, and crosses the aortic valve into the aorta before it divides—at the region of the descending aorta (if there is a patent ductus arteriosus) or in the ascending aorta (*if* there is an aortoseptal defect). Therefore, the aorta is dilated in aortopulmonary shunts, whereas it is not when the shunt is at the atrial or ventricular level.

To summarize these observations, the presence of left ventricular enlargement differentiates shunts distal to the AV valves from those at the atrial level, and the presence of aortic enlargement differentiates shunts distal to the aortic valve from those at the ventricular level.

Associated valvular deformities modify these findings. Furthermore, combinations of anomalies, such as ventricular septal defect plus patency of the ductus or coarctation of the aorta, occur with sufficient frequency that one cannot expect to reach an exact anatomic diagnosis each time from radiologic studies. Each series of films, however, is a new challenge to detect the changes present and to offer the most reasonable explanations for the observed manifestations.

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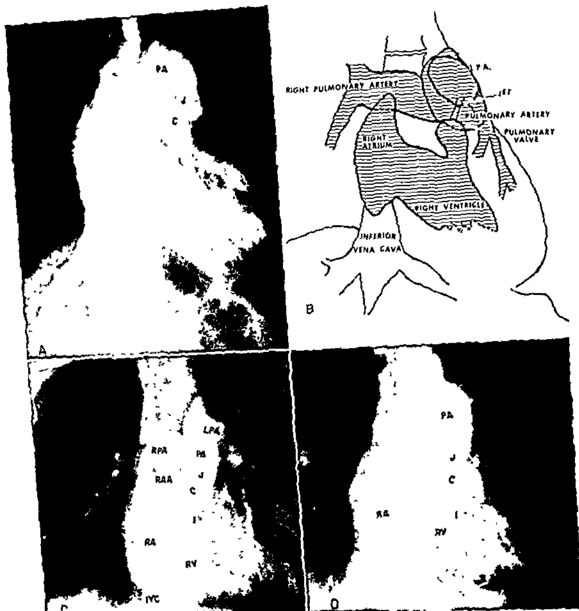


Fig 6-71. A. Isolated valvular pulmonic stenosis *in a 22-year-old woman with pressures of* 194/8 mm Hg in the right ventricle and 13/3 in the pulmonary artery. A Frontal angiocardiogram, 2½ sec after the beginning of injection shows the infundibulum (I) of the right ventricle to *be widely patent* The pulmonary cusps (C) are clearly outlined, and the jet (J) entering the poststenotic pulmonary *artery (PA) is evident. The peripheral* pulmonary vascular tree is markedly decreased. B. Tracing of (A). C Isolated pulmonic valvular stenosis *in a 27-year-old woman* with pressures of 175/25 mm Hg in the right ventricle and 25/5 in the pulmonary artery The right atrium (*RA*), inferior vena cava (*IVC*), right ventricle (*RV*), infundibulum (*I*), pulmonic cusps (*C*), *pulmonary artery (PA), right (RPA) and left (LPA) branches of the pulmonary artery are* opacified. Note the jet (J) directed into the poststenotic *dilated pulmonary* artery. The infundibulum is in systole; its contracted state simulates stenosis. The peripheral *pulmonary arterial tree is diminished.* D. Valvular pulmonic stenosis and atrial septal defect *in a 34-year-old woman* with arrested *pulmonary tuberculosis. Right* ventricular hypertension, 96/15; pulmonary artery mean pressure, 10 mm Hg The right *atrium (RA) is in diastole;* the right ventricle (RV) with its outflow tract, the infundibulum (I), is also contracted because of systole. *Note the pulmonic cusps (C) with the jet (J)* streaming into the poststenotic pulmonary artery (PA). The pulmonary *vasculature* is markedly *decreased.* The narrowed infundibulum simulates stenosis. Other films demonstrated right-to-left shunt through an atrial *defect.*

but with a normal-appearing heart and great vessels. From the patient's standpoint, this is probably a favorable situation, meaning that his lesion is so mild it has not altered cardiac dynamics enough to make its presence felt. But from the point of view of the physician interested in a diagnosis, this can be frustrating. Small patent ductus, small ventricular septal defect, slight pulmonic or aortic stenosis, etc., are among the possibilities.

If there is enlargement of some chamber or vessel, one has more to go on. It is helpful then to decide how far the enlargement extends to the structures proximal and distal to the one involved. For example, if the right atrium is prominent and the right ventricle is enlarged, one analyzes the pulmonary arteries and left side of the heart for evidence of involvement. If the main pulmonary artery is then found to be enlarged, but the pulmonary artery branches are not and the left side of the heart is normal, this points to *valvular pulmonic stenosis* with poststenotic dilatation of the main pulmonary artery and with enlargement of the right side of the heart as a result of the obstruction (Fig. 6-58). If not only the main pulmonary artery but also the branches throughout the lung fields are found engorged and actively pulsating while the left side of the heart is normal, this implies a lesion producing *overcirculation* through the right heart chambers and pulmonary vascular tree. an atrial septal defect, an anomalous pulmonary venous drainage, or both (Fig. 6-61)

If in addition to enlargement of the right heart chambers, main pulmonary artery, and branches, there is moderate enlargement of the left atrium but not of the left ventricle (a point sometimes difficult to determine), *mitral valvular obstruction* is implicated

If the enlargement includes the left ventricle besides, but the aorta is normal or small, several possibilities are suggested. For instance, a lesion of the mitral valve with insufficiency and often also with stenosis, or endocardial or myocardial involvement of the left ventricle with secondary changes in the lungs and right heart, as in *endocardial fibroelastosis, myocarditis, anomalous origin of the left coronary artery,* or *glycogen storage disease of the heart.* If the pulmonary arterial engorgement is noteworthy and pulsations of the vessels are increased, *ventricular septal defect* is likely (Fig. 6-62).

If the enlargement involves the aorta, in addition to the chambers and vessels proximal to it, this places the lesion *at the aortic valve* or beyond, e.g., aortic stenosis, insufficiency, or both or coarctation of the aorta (Figs. 6-66 and 6-67). If there is pulmonary overcirculation, then *patent ductus arteriosus* (or the rare aortic septal defect) is the probable diagnosis (Fig. 6-63).

Patients with left-to-right shunts producing increased pulmonary blood flow present a frequent problem in differential diagnosis of the site of the shunt. The accompanying schematic diagram (Fig. 6-60) illustrates some useful points in differentiation if the shunt is large enough to cause a detectable change in chamber and vessel size. The electrocardiographic expression of ventricular hypertrophy or dilatation is shown alongside the appropriate ventricle Particularly for infants in difficulty because of the large left-to-right shunt, these differential features have been useful.

For comparison, the normal situation is illustrated at the upper left, where each side of the heart carries the same volume of blood and the internal dimensions of chambers and vessels are comparable on the two sides The thickness of the two ventricles is the chief difference, a reflection of the differences in peripheral resistances in the pulmonary and systemic circuits

In the other three conditions, the pulmonary blood flow is increased above normal by the left-to-right shunt, and the pulmonary artery is enlarged in all. It is what happens to this increased volume of blood after it returns from the lungs that determines the changes to be described.

When the shunt is *at the atrial level,* a large portion of the blood coming to the left atrium passes across the defect into the right atrium and a smaller amount takes the normal route across the mitral valve to the left ventricle The disproportionate division is believed related to the greater distensibility of the right atrium and right ventricle, which offer less resistance to flow than do the more tense left atrium and left ventricle. If there is *anomalous pulmonary venous drainage* from the lungs, the right atrium (directly or through one of its tributaries) receives a supernormal

were markedly enlarged. In two patients with a patent ductus arteriosus, there was left atrial enlargement, enlargement of the pulmonary artery and right ventricle, with reversal of flow through the ductus due to pulmonary hypertension.

Coarctation of the Aorta. Angiocardiography in coarctation of the aorta is customarily performed in the LAO projection, which affords an open view of the aortic arch similar to surgical exposure The angiocardiographic findings are as follows. The left ventricle may be enlarged. The ascending aorta, often normal in young patients, is usually dilated in the adult. The innominate and left subclavian arteries are often markedly dilated, the left common carotid artery is moderately enlarged Collateral channels, particularly the internal mammary and shoulder girdle arteries, are markedly dilated and tortuous The intercostal arteries are not as well visualized. The exact site of coarctation is readily identified at a variable distance beyond the left subclavian artery (Fig 6-73A) There is an area of abrupt constriction which is obscured in part by overlapping of the poststenotic segment of the aorta. The diameter of the lumen at the site of coarctation cannot be determined. Prompt filling of an aorta distal to the stenosis may occur via collaterals in the absence of any opening. The length of the stub of aorta distal to the left subclavian artery and proximal to the site of stricture varies, ranging between no stub to a 4.5-cm segment Dilated intercostal arteries may occasionally be seen connecting with the poststenotic descending aorta Occasionally aneurysms of the intercostal vessels can be recognized. *Poststenotic aortic dilatation* varies greatly and is generally more marked in older patients; the lower thoracic aorta is usually small

Aneurysmal dilatation of the aortic sinuses associated with coarctation of the aorta has been recognized *Pseudocoarctation*, a congenital type of kinking of the aorta, closely resembles coarctation of the aorta Indeed, the angiocardiographic studies may duplicate the findings seen in coarctation of the aorta. The differentiation from a true coarctation depends upon the absence of arterial collaterals and normal lower extremity blood pressures (*Steinberg, 1956*).

SIMPLE SHUNTS

Atrial Septal Defects. The angiocardiogram reveals right heart and pulmonary arterial enlargement. Contrast agents can sometimes be seen to pass from the right to the left atrium. *Filling defects* due to left-to-right shunting of blood may often be recognized in the right atrium. Associated defects such as pulmonary stenosis, tricuspid atresia, and anomalous drainage of pulmonary veins are frequently accompanied by right-to-left atrial shunts. The usual finding is that of *persistent opacification of the right atrium, right ventricle,* and *pulmonary arteries* which lasts during the entire period of cardiac filling and results from recirculation of opacified blood from the left to the right atrium. Opacification of the chambers of the left heart and aorta is usually of poor quality because of dilution of the contrast agent by large volumes of shunted blood. Persistent opacification of the pulmonary arteries also occurs as a result of a large ventricular septal defect, patent ductus arteriosus, and defects in the aortopulmonary septum, but the right atrium does not share in the opacification. It is occasionally difficult to establish with certainty that recirculation of contrast agent is actually present A slow injection or the trapping of contrast agent in the arm or neck veins may result in prolonged filling of the right atrium and lead to a mistaken angiocardiographic diagnosis of atrial defect

Ventricular Septal Defects. Angiocardiography may show no abnormality in the presence of small defects in the ventricular septum There may be evidence of *reopacification of the right ventricle* (but not the right atrium) at the time of left heart filling, but as is a case with atrial defects, the finding is difficult to evaluate. In high ventricular septal defects there may be angiocardiographic demonstra-

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90/72, has had severe precordial pain for 10 years. The left ventricle (*LV*) is moderately enlarged The ascending aorta is markedly dilated and measures 50 *mm* in the mid-ascending portion (average normal, 28 mm) There is also moderate dilatation of the brachiocephalic arteries (*A*, innominate, *LCC*, left common carotid, *LSA*, the left subclavian arteries

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Angiocardiography in congenital heart disease

ISRAEL STEINBERG

STENOSIS OF A VALVE OR VESSEL

Pulmonic Stenosis. There are two main types of pulmonary stenosis, the valvular and infundibular. The *valvular* types (Fig 6-71) consist of a dome-shaped membranous opened, umbrella-like structure formed by the fused pulmonic cusps. An orifice, usually centrally located, can be identified by a "jet" of opacified blood. The valve cusps are mobile despite fusion and are easily identified, especially during diastole. The right ventricle is enlarged, and during diastole, thickening and trabeculation of the wall can be recognized (Fig 6-71). The outflow tract of the right ventricle is of good caliber during systole (Fig. 6-71) but may appear contracted and simulate infundibular stenosis during diastole. The main stem pulmonary artery has often a characteristic *poststenotic dilatation* (Fig 6-71). The peripheral branches may be normal but are usually reduced in size. *Supravalvular pulmonic stenosis* is rare (Fig. 6-72A). *Multiple stenosis of the pulmonary arteries*, chiefly the main branches, has recently been reported and called "coarctation of the pulmonary arteries."

Infundibular stenosis of the pulmonary artery rarely occurs as an isolated lesion. Usually it is associated with deformities of the ventricular septum, occurring in the tetralogy of Fallot and in transposition.

Aortic Stenosis. Aortic stenosis may be divided into the valvular and subvalvular types. In the *valvular* types, the cusps are thickened and may be fused to form a dome-shaped diaphragm with a central opening. Frequently, there is *poststenotic dilatation* of the ascending aorta. Whether valvular stenosis is here a truly developmental anomaly or is the result of endocardial fibroelastosis is difficult to decide clinically (Nadas). It is almost impossible to distinguish between aortic valvular and subaortic types, even after angiocardiography. Figures 6-72C and 6-73A, B show dome-shaped deformities of the aortic cusps with poststenotic dilatation of the ascending aorta. Figure 6-72B shows the angiocardiogram of a puppy who had all the physical signs of aortic stenosis; the diagnosis was confirmed at operation. The angiocardiograms of congenital aortic valvular stenosis in a child (Fig. 6-72C) and in an adult (Fig 6-72D) are also illustrated.

Mitral Stenosis. Congenital mitral stenosis is rare, but associations with aortic valve, aorta, and ductus arteriosus malformations are not uncommon (Ferencz et al.). In the angiocardiogram, isolated enlargement and delay in emptying of the left atrium, and enlargement of the right ventricle and pulmonary artery are seen in uncomplicated mitral stenosis. In one patient who had partial anomalous drainage from the right lung into the superior vena cava and an atrial septal defect (Lutembacher's syndrome), the left atrium was hypoplastic and the pulmonary arteries, pulmonary vascular tree, and right ventricles

tion of shunting of blood in both directions across the defect, especially with pulmonary hypertension. Even after cardiac catheterization, it may be difficult in certain cases to distinguish between such a lesion and the Eisenmenger complex

Patent Ductus Arteriosus. The angiocardiographic findings which have been observed in patients with patent ductus arteriosus include (1) dilation of pulmonary arteries, (2) high position of the left pulmonary artery, (3) a defect in the column of contrast substance within and at the time of filling of the pulmonary artery and left pulmonary artery caused by a "jet" of nonopacified blood issuing from the ductus (Fig 6-73B), (4) persistent opacification of the pulmonary arteries at the time of aortic filling (Fig 6-73C), (5) localized dilatation of the aorta at the site of origin of the ductus, and (6) rarely, opacification of the ductus itself These signs have all been absent in some proved cases of patent ductus arteriosus Thoracic aortography reveals the anatomy of patent ductus arteriosus with clarity (Kjellberg et al, 1955), but its routine use is not justified since the diagnosis can usually be established by the stethoscope

In some cases of patent ductus, the pulmonary arterial blood pressure may be elevated to systemic levels When this occurs, the direction of flow across the ductus becomes reversed, with the production of typical clinical and angiocardiographic findings As illustrated in Fig 6-73B, early opacification of the descending (but not the ascending) aorta occurs Later films show opacification of the ascending aorta and rule out the presence of stenosis of the aortic arch As would be expected, this situation results in cyanosis localized to the lower but not the upper extremities (Lukas et al)

Aortic Septal Defect. Since patent ductus and aortoseptal defects produce the same hemodynamic abnormality, it is usually not possible to distinguish them by means of angiocardiography. Fortunately, the latter lesion is rare. The diagnosis may be suspected clinically and confirmed by thoracic aortography. Such a defect has been occasionally repaired, although in general it must be considered an inoperable condition.

COMBINED MALFORMATIONS

Pulmonic Stenosis plus Atrial Septal Defects. In the presence of a combined pulmonary stenosis and a defect in the atrial septum, an overriding aorta may be simulated on angiocardiography. In this malformation, blood passes across the septal defect from the right to the left atrium, via the left ventricle into the aorta, while at the same time blood entering the right ventricle through the tricuspid valve reaches the lungs through a stenotic pulmonary artery. Cyanosis results. Angiocardiography may reveal simultaneous opacification of the aorta and the pulmonary artery. The diagnosis of dextroposition of the aorta is made less likely by the demonstration of a direct passage of contrast agent from the right to the left atrium on early films of the series This finding is not conclusive since an atrial defect with reversal of flow may sometimes complicate the tetralogy of Fallot. Reflux of contrast agent into the inferior vena cava is common in this condition as in tricuspid stenosis or atresia but may also occur normally In pulmonary stenosis and atrial septal defect, the pulmonary arteries usually show poststenotic dilation and are emptied of contrast substance more slowly than is the aorta Especially, when the pulmonary stenosis is severe, cyanosis may be present from birth In other cases, cyanosis may be delayed in onset. This is because the pulmonary stenosis over a period of years has resulted in a gradual elevation of the right ventricular end-diastolic and hence the right atrial pressure When the latter exceeds the pressure in the left atrium,

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reopacification (arrow) of the left pulmonary artery. D Frontal angiocardiogram of a 4-month-old infant with cyanosis of the lower trunk and extremities and murmurs of aortic stenosis. When the right heart structures—right atrium (RA), right ventricle (RV), pulmonary artery (PA)—were opacified, there was reversed blood flow through a patent ductus arteriosus (white arrow) into the descending aorta (AO) The abdominal aorta (black arrow) contains unsaturated pulmonary arterial blood and is responsible for the lower trunk and extremity cyanosis. Ligation of the ductus resulted in improvement for 3 days Death was sudden At necropsy, fibroelastosis of the left ventricle with aortic stenosis was found



Fig. 6-72. A. Stenosis of right pulmonary artery in a 4-year-old child, with pulmonic valvular stenosis. Cardiac catheterization showed right ventricle pressure of 60/6, pulmonary artery (mean) pressure, 10 mm Hg. There was no pressure change on withdrawal of the catheter from the right pulmonary artery However, stenosis (arrow) of the right pulmonary branch is clearly seen in the angiocardiogram. B. Aortic valvular stenosis, confirmed by operation, in a 4-month-old German shepherd dog. Note the dome-shaped aortic cusps (arrow) with the poststenotic ascending aorta (AO). C. Valvular stenosis in a 9-year-old boy with a history since birth of a systolic murmur transmitted to the neck. The left atrium (LA) and left ventricle (LV) are opacified. Note the deformed aortic cusps (arrow) and the poststenotic dilated ascending aorta (AO) which measures 4 cm in diameter (normal 25 mm) Previous angiocardiogram 3 years earlier also showed deformed aortic cusps and poststenotic dilatation of the aorta. D. Valvular aortic stenosis in a 27-year-old woman with a history of an aortic systolic murmur since birth Blood pressure is

Angiocardiography, by showing *marked lateral* displacement of the tricuspid valve membrane, often establishes the diagnosis. Usually there is a slight notch along the inferior border of the heart well toward the left cardiac silhouette (Fig 6-74A). Marked dilatation of the right atrium and the proximal portion of the right ventricle forming a common chamber *may also be detected* The atrialized portion of the ventricle may also be markedly thinned. Prolonged opacification of the right cardiac chamber is usual, with hypoplasia of the main pulmonary artery and its stems. The peripheral pulmonary arterial tree is strikingly decreased and poorly opacified (Fig. 6-74A). In about 60 per cent of the cases, right-to-left filling of the atria can be demonstrated, indicating either a patent foramen ovale or an atrial septal defect

Mitral Stenosis plus Atrial Septal Defect (Lutembacher's Syndrome). The combination of rheumatic mitral stenosis with an atrial septal defect (Lutembacher's syndrome), while uncommon, is not so rare as the congenital type of mitral stenosis with atrial septal defect In one case, angiocardiography revealed a "jet sign" at the insertion of the anomalous veins of the right lung and demonstrated an atrial septal defect but failed to detect the mitral stenosis; hypoplasia of the left atrium was in marked contrast to the usual enlargement of this structure

COMPLEX MALFORMATIONS

Tetralogy and Pentalogy of Fallot. Tetralogy of Fallot consists essentially of the combination of two lesions, pulmonary stenosis (infundibular or valvular) and dextroposition or overriding of the aorta A physiologic, if not an anatomic, ventricular septal defect always occurs when the aorta overrides the ventricular septum, while right ventricular hypertrophy is the result of pulmonary stenosis.

The angiocardiographic identification of *pulmonary stenosis* may be direct or indirect Selective angiocardiography has considerably increased the direct diagnosis of pulmonary stenosis (Kjellberg et al, 1955) In only about half the cases, the pulmonary infundibular or valvular narrowing is seen with the intravenous method. The presence of stenosis may, however, be inferred with reasonable assurance from *one* or more of the following findings: (1) the peripheral pulmonary *arteries are unusually small*; (2) they fill poorly with opaque *substance*; and (3) the central pulmonary arteries, even though *fairly* large and well filled, are *irregularly* deformed in appearance, while the peripheral branches are disproportionately *small*. Even though good filling of apparently normal pulmonary arteries is seen, pulmonary stenosis cannot be excluded angiocardiographically (although in such cases it is reasonable to conclude that marked reduction in pulmonary blood flow is not present). Furthermore, failure of the pulmonary arteries to fill with contrast substance may be the result of transposition of the great blood vessels rather than pulmonary stenosis.

Dextroposition or overriding of the aorta is manifest in the angiocardiogram by the immediate passage of contrast agent from the right ventricle into the aorta, a direct demonstration of the cause of the patient's cyanosis. In general, the degree to which the aorta overrides can be estimated from two findings. If early aortic opacification is faint as compared to the density in the pulmonary artery and as compared to that obtained later in the angiocardiographic series when contrast substance reaches the aorta from the left ventricle, it may be assumed that but slight dextroposition exists Furthermore, the position of the base of the aorta with respect to the heart border and the contour of the aortic arch are of significance The farther anterior the origin of the aorta and the more rounded out its course throughout the thorax, the greater is the degree of aortic overriding (Fig 6-74B).

The so-called *pseudotruncus arteriosus* is a variant of the tetralogy of Fallot in which the pulmonary artery is markedly *stenotic* if not atretic, circulation to the lungs being via bronchial arteries.

Angiocardiography readily demonstrates associated anomalies of the aortic arch *and* branches. A *right aortic arch* and the position of the branches may be *often* a determining factor in the type of aortopulmonary surgery, *i e*, whether the Potts or Blalock-Taussig operation is done (Cooley et al, 1949).

Pentalogy of Fallot. In the pentalogy of Fallot, the angiocardiographic findings are essentially as *in the tetralogy*, with the addition of an atrial septal defect. This is *demonstrated*



Fig. 6-72. A Stenosis of right pulmonary artery in a 4-year-old child, with pulmonic valvular stenosis. Cardiac catheterization showed right ventricle pressure of 60/6; pulmonary artery (mean) pressure, 10 mm Hg. There was no pressure change on withdrawal of the catheter from the right pulmonary artery. However, stenosis (arrow) of the right pulmonary branch is clearly seen in the angiocardiogram. B. Aortic valvular stenosis, confirmed by operation, in a 4-month-old German shepherd dog. Note the dome-shaped aortic cusps (arrow) with the poststenotic ascending aorta (AO). C. Valvular stenosis in a 9-year-old boy with a history since birth of a systolic murmur transmitted to the neck. The left atrium (LA) and left ventricle (LV) are opacified. Note the deformed aortic cusps (arrow) and the poststenotic dilated ascending aorta (AO) which measures 4 cm in diameter (normal 25 mm) Previous angiocardiogram 3 years earlier also showed deformed aortic cusps and poststenotic dilatation of the aorta D Valvular aortic stenosis in a 27-year-old woman with a history of an aortic systolic murmur since birth Blood pressure is

pulmonary artery partially overrides the ventricular septum A high ventricular septal defect and right ventricular hypertrophy complete the syndrome (Chiechi). The diagnostic angiocardiographic feature consists of simultaneous filling of the dilated pulmonary artery and aorta, differentiating it from the ordinary transposition. However, this is not pathognomonic since transposition with a large ventricular septal defect can produce the same picture. Outlining the ventricular septum with a clear origin of the pulmonary artery from both ventricles and transposition of the aorta are essential for diagnosis of the Taussig-Bing complex.

Tricuspid Atresia. In tricuspid atresia, blood flow is from the right atrium across an atrial defect into the left ventricle and then into the aorta and pulmonary arteries, often via a ventricular septal defect into a rudimentary pulmonary conus. The origin of the great vessels may vary considerably. Both may arise

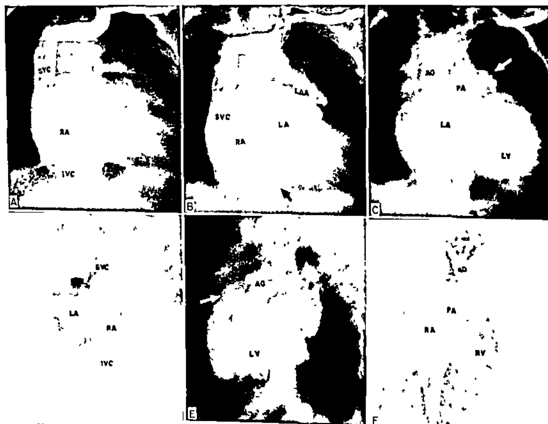


Fig 6-76 Tricuspid atresia and pulmonary stenosis in a 3-year-old child (verified at autopsy) A. Frontal angiocardiogram showing early filling of the right atrium (RA) from the superior vena cava (SVC) The inferior vena cava (IVC) is filled refluxly. B Shortly thereafter, there is filling of the left atrium (LA) and left atrial appendage (LAA). Arrow points to the hypoplastic right ventricle C Later, the left atrium (LA), left ventricle (LV), aorta (AO), and pulmonary artery (PA) are opacified The deformed and poorly filled pulmonary artery and branches (arrow) are indications of decreased pulmonary blood flow. D The early lateral angiocardiogram shows opacification of the right atrium (RA), superior vena cava (SVC), inferior vena cava (IVC), and left atrium (LA). E. Later, there is filling of the aorta (AO) and left ventricle (LV). The pulmonary artery is vaguely outlined and the pulmonary vasculature is markedly decreased. F. Frontal angiocardiogram of a 5-month-old cyanotic infant with mitral atresia (verified at autopsy) reveals simultaneous filling of the right atrium (RA), right ventricle (RV), pulmonary artery (PA), and aorta (AO) The unfilled left lower cardiac shadow (arrow) represents the nonfunctioning rudimentary left ventricle. Death from heart failure ensued, and a patent ductus arteriosus and coarctation of the aorta were found at autopsy The opacified descending aorta was apparently filled from the pulmonary artery by reversed flow through the ductus.



Fig. 6-73. A. Left anterior oblique angiocardiogram in a 24-year-old woman with mild hypertension (142/80) of the upper and hypotension (75/0) of the lower extremities. The left ventricle (LV) is normal in size. The ascending aorta (AO) is mildly dilated. The brachiocephalic arteries—the innominate (IA), left common carotid (LCCA) and the left subclavian (LSA)—are only slightly dilated. The site of coarctation (arrow) is just below the aortic arch. The collateral arterials are only mildly dilated, operation was postponed. B. Patent ductus arteriosus in a 19-year-old woman. Frontal angiocardiogram shows the opacified right heart. A tiny rounded area (arrow) in the left pulmonary artery is a "jet" of unopacified blood from a patent ductus arteriosus. C. When the left heart chambers, left atrium (LA), left ventricle (LV), and aorta (AO) are opacified, there is

pulmonary artery partially overrides the ventricular septum. A *high ventricular septal* defect and right ventricular hypertrophy complete the syndrome (Chiechi). The diagnostic angiocardiographic feature consists *of* simultaneous filling of the dilated pulmonary artery and aorta, *differentiating* it from the ordinary transposition. However, this is not pathognomonic since transposition with a large ventricular *septal defect* can produce the same picture. Outlining the ventricular septum *with* a clear origin *of the* pulmonary artery from both ventricles and transposition of the aorta are essential for diagnosis of the Taussig-Bing complex.

Tricuspid Atresia. In tricuspid atresia, blood flow *is from the* right atrium across an atrial defect into the left ventricle and then into the aorta and pulmonary *arteries*, often via a ventricular *septal* defect into a rudimentary pulmonary conus. The origin *of the great* vessels may vary considerably. Both may arise

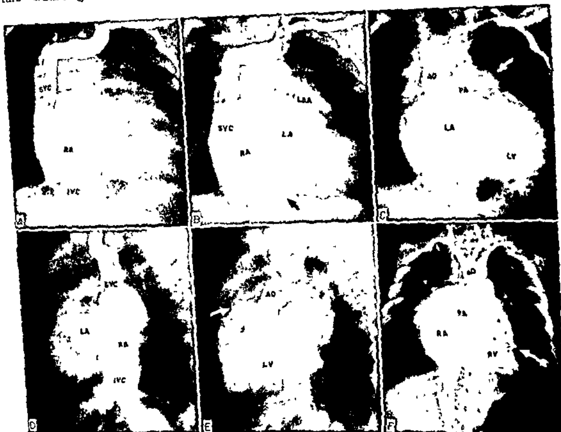


Fig. 6-76 Tricuspid atresia and pulmonary *stenosis* in a 3-year-old child (verified at *autopsy*) A. Frontal angiocardiogram showing early filling of the *right atrium* (RA) *from* the superior vena cava (SVC). The inferior vena cava (IVC) is filled refluxly. B. Shortly thereafter, there is filling of the *left atrium (LA) and left* atri... tricle. C. Later, the left atrium (LA), ... opacified. The deformed and poor... of decreased *pulmonary* blood flow. D. The early *lateral angiocardiogram* shows opacification of the right atrium (RA), superior vena cava (SVC), *inferior* vena cava (IVC), and left atrium (LA). E. Later, there is filling of the aorta (AO) and *left ventricle* (LV). The pulmonary artery *is vaguely outlined* and the pulmonary vasculature is markedly decreased. F. Frontal *angiocardiogram* of a 5-month-old cyanotic infant with mitral atresia (verified *at autopsy*) *reveals* simultaneous filling of the right atrium (RA), right ventricle (RV), pulmonary artery (PA), and aorta (AO). The unfilled left lower cardiac shadow (arrow) *represents the* nonfunctioning rudimentary left ventricle. Death from heart failure ensued, and a patent ductus arteriosus and coarctation of the aorta were found at autopsy. The opacified descending aorta was *apparently* filled from the pulmonary artery by *reversed* flow through the ductus.





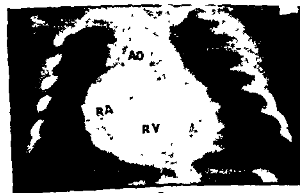


Fig. 6-74. A. Frontal angiocardiogram of a 19-year-old woman with Ebstein's anomaly (confirmed by cardiac catheterization). The superior vena cava (SVC) is widened; the right atrium (*RA*) is huge, and the right ventricle (*RV*) is divided at the notch (arrow), the site of the tricuspid membrane, into proximal and distal chambers. The outflow tract of the right ventricle is poorly defined; and the pulmonary artery and branches are hypoplastic and unopacified B Frontal angiocardiogram of a 5½-year-old child with tetralogy of Fallot. The classical features of the complex are readily seen. There is simultaneous opacification of the pulmonary artery (*PA*) and *aorta (AO)*. The right ventricle (*RV*) is large, the infundibulum (*I*) is stenotic (arrow), and there is *poststenotic dilatation* of the pulmonary artery with *diminished* pulmonary vasculature, especially within the *right lung*. *C*. Frontal angiocardiogram of a 4-month-old infant with complete *transposition* of the *great vessels*, confirmed at autopsy. The right atrium (*RA*) *is normal* in size. The right ventricle (*RV*) is large, and the aorta (*AO*) is seen arising from it

reversed flow across the defect (usually a patent foramen ovale) occurs and cyanosis results.

Aortic Stenosis plus Coarctation of the Aorta or Patent Ductus Arteriosus. The occurrence of aortic stenosis and a patent ductus arteriosus or coarctation of the aorta is uncommon. In a patient with fibroelastosis of the left ventricle and aortic valvular stenosis, the angiocardiogram showed a markedly enlarged left ventricle (cavity and wall) with delay in emptying. There was also marked dilatation of the ascending aorta, which terminated abruptly beyond the left subclavian artery and simulated coarctation of the aorta. Caution is advised in marking the diagnosis of coarctation of the aorta in the presence of aortic stenosis unless there is unequivocal clinical evidence of coarctation, such as the corroborative findings of diminished or absent femoral arterial blood flow. Reversal of flow through a patent ductus resulted when fibroelastosis of the heart and aortic stenosis were associated with marked pulmonary hypertension (Fig 6-73D).

Tricuspid Insufficiency (Ebstein's Anomaly). Ebstein's anomaly consists of fusion of the tricuspid leaflets into a membranous structure extending into the cavity of the right ventricle, forming proximal and distal chambers. The proximal chamber becomes continuous with the right atrium; the distal chamber functions as the right ventricle. An atrial septal defect, either a patent foramen ovale or true atrial septal defect, may also be present and cause cyanosis. Usually the wall of the proximal portion of the ventricle (the atrialized chamber) is thinned The rest of the ventricle is often hypertrophied



Fig. 6-77. Upper left, congenital absence of the right pulmonary artery. Frontal angiocardiogram of an asymptomatic 24-year-old man shows opacification of the superior vena cava (SVC), right atrium (RA), right ventricle (RV), infundibulum (I), pulmonary artery (PA), and left pulmonary artery (LPA). The right pulmonary artery is congenitally absent. A later film at the time of aortic opacification revealed a fine lacelike pattern of pulmonary vasculature in the right lung, presumably coming from bronchial arteries. Upper right, frontal angiocardiogram of a 24-year-old asymptomatic man with congenital absence of the left pulmonary artery. The right ventricle (RV), pulmonary artery (PA) and right pulmonary artery (RPA) are opacified. The left pulmonary artery is congenitally absent. Later, the left lung became opacified from bronchial arteries. Lower left, agenesis of the left lung with reversal of blood flow through a patent ductus arteriosus in a 22-year-old man. Angiocardiogram shows the enlarged right ventricle, pulmonary artery with the patent ductus arteriosus, and opacified descending aorta. The left pulmonary artery is absent. Lower right, tracing of (A).

by right-to-left flow from the right to left atrium.

Eisenmenger's Complex. In this anomaly, there is an overriding aorta associated with pulmonary hypertension. Angiocardiographically, the overriding aorta and pulmonary artery are often filled simultaneously from the right ventricle. However, with a slight degree of overriding the aorta may be only faintly filled. The differential diagnosis between Eisenmenger's complex and a high ventricular septal defect is made with great difficulty, even after cardiac catheterization Marked enlargement of the main trunk of the pulmonary artery and dilatation of the pulmonary and peripheral branches with dense opacification are usually present (Ebnotha and Abrams).

Transposition of the Great Blood Vessels. It may be difficult to distinguish with certainty between extreme dextroposition of the aorta associated with severe pulmonary stenosis and complete transposition of the aorta and pulmonary artery, particularly when pulmonary stenosis complicates transposition. The aorta in transposition "takes off" far anteriorly and describes an open, rounded course through the upper thorax (Figs. 6-74C and 6-75). The density of contrast substance within the aorta closely approximates that within the right ventricle (Fig. 6-74C). If the pulmonary arteries appear prominent in the conventional roentgenogram or unusually pulsatile at fluoroscopy and yet fill poorly or not at all during angiocardiography, transposition of the aorta and pulmonary artery should be strongly suspected (Fig. 6-75). When pulmonary stenosis is present, the diagnosis may be more difficult. Although, in transposition of the great blood vessels, life is dependent upon some intercommunication between the systemic and pulmonary circuits, these communications are rarely demonstrated by angiocardiography

Taussig-Bing Syndrome. In this anomaly, a transposed aorta and a large pulmonary artery arise primarily from the right ventricle; the

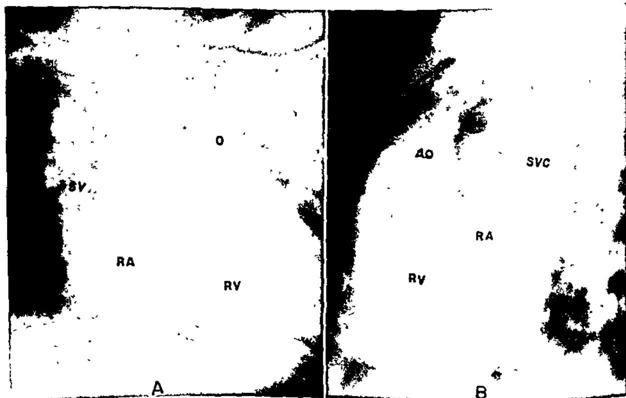


Fig. 6-75. Complete transposition of the great vessels in a 2-year-old infant A Frontal angiocardiogram shows the right heart, superior vena cava (SV), right atrium (RA), and right ventricle (RV) opacified. The aorta (O) arises from the right ventricle B Lateral angiocardiogram reveals the right heart structures, the superior vena cava (SVC), right atrium (RA), and right ventricle (RV). The aorta (AO) arises from the right ventricle and sweeps forward just behind the sternum and arches posteriorly to descend well along the spine. Later, poor filling of the pulmonary artery arising from the left ventricle was recognized.

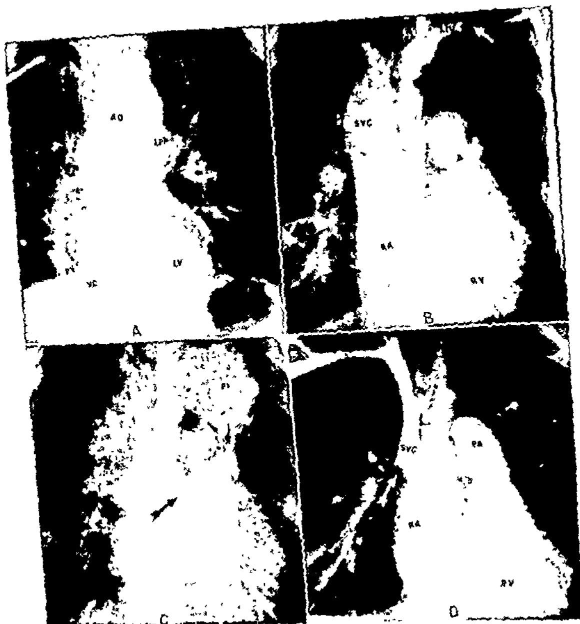


Fig. 6-79 A. Frontal an[illegible]
age of the right pulmonary [illegible]
of the right pulmonary veins, left ventricle (LV), and aorta (AO), there was [illegible]
pulmonary artery and branches. The left branch (LPA) is especially well delineated. B. Total anomalous pulmonary venous drainage into the left innominate vein in a 42-year-old woman. There is a filling defect (arrow) in the left innominate vein (LIV) due to a stream of blood from the anomalous pulmonary veins. The right superior vena cava (SVC) is markedly dilated and forms a right mediastinal mass. The right atrium (RA), right ventricle (RV), and pulmonary artery are also enlarged. C. Later, the pulmonary veins of both lungs form a common channel (arrow) which inserts via a huge structure, probably a persistent left superior vena cava (PV) which is responsible for the left superior mediastinal mass. D. Total anomalous pulmonary venous drainage of pulmonary veins into the junction of the superior vena cava and right atrium in a 16-year-old girl. There is a filling defect (arrow) at the junction of the superior vena cava (SVC) and right atrium (RA) caused by a "jet" of unopacified blood from pulmonary veins. The right ventricle (RV) and pulmonary artery (PA) are enlarged.

from the left ventricle; either may arise from a diminutive right ventricle which receives blood from the left ventricle via a ventricular septal defect. Pulmonary stenosis may occur, as may an associated patent ductus arteriosus (Cooley et al., 1950). Angiocardiography usually reveals the abnormal course of blood flow clearly (Fig. 6-76) In this example the aorta takes origin from a diminutive, nonfunctioning right ventricle (filled via an interventricular septal defect), while the small pulmonary arteries give evidence of pulmonary stenosis. In another case (Dotter and Steinberg, 1951), tricuspid atresia was associated with dextrocardia, a common atrium, an anomalous pulmonary vein entering a left superior vena cava, a functioning single ("left") ventricle, severe pulmonary stenosis, and a large patent ductus through which blood reached the lungs All the anatomic features, except the tricuspid atresia, were clearly shown in the angiocardiogram. Since the diagnosis of tricuspid stenosis or atresia may be considered likely when cyanosis and left axis deviation occur together, angiocardiography need be employed only when surgical procedures are contemplated or in atypical cases.

Mitral Atresia plus Patent Ductus and Coarctation of the Aorta. A cyanotic infant showed (Fig. 6-76F) almost immediate filling of the right heart and aorta At autopsy there was mitral atresia, coarctation of the aorta, and a patent ductus arteriosus The angiocardiogram was striking because all the cardiovascular structures, save the functionless hypoplastic left ventricle, were opacified, the patent ductus could not be recognized with certainty

ANOMALIES OF THE LARGE ARTERIAL VESSELS

Primary Dilatation (Aneurysm) of the Pulmonary Artery. Idiopathic or primary dilatation of the pulmonary artery is rare Angiocardiography readily demonstrates enlargement of the pulmonary artery However, the diagnosis of primary dilatation of the pulmonary artery can be made only when the many causes of pulmonary artery dilatation, such as pulmonic stenosis, congenital heart disease, rheumatic heart disease, cor pulmonale, heart failure, and syphilis, are excluded. Primary dilatation without hypertension rarely causes disability and requires no treatment.

Absence of a Main Stem of the Pulmonary Artery. Either a right or left main stem of the pulmonary artery may be congenitally absent, and the diagnosis can often be made by conventional roentgenography. There is displacement of the mediastinum (mediastinal herniation), trachea, and heart by an overdistended lung, while the opposite lung is hypoplastic and poorly vascularized. The angiocardiographic study demonstrates the absence of a pulmonary artery with good vascularity of the overdistended lung (Fig. 6-77, upper left). Studies utilizing rapid serial roentgenography have disclosed that the bronchial arterial circulation supplies the poorly vascularized lung.

Experience in three cases indicates that absence of a main branch, when uncomplicated, is usually discovered during routine chest x-ray survey. The condition may be mistaken for a mediastinal tumor. Absence of a main branch has also been recently described in association with cyanotic congenital heart disease, usually tetralogy of Fallot.

Absence of a Lung (Agenesis). Absence of a main branch of the pulmonary artery also occurs in lung agenesis. Differentiation from an acquired fibrothorax depends upon the demonstration by bronchography or bronchoscopy of a congenitally absent bronchus. The diagnosis should be suspected if there is an opaque, shrunken hemithorax containing the mediastinal structures, heart, and great blood vessels without a main bronchus. In a 22-year-old patient, in addition to absence of the left pulmonary artery, there was a markedly enlarged pulmonary artery and right branch due to pulmonary hypertension and a patent ductus arteriosus with reversal of flow (Fig. 6-77, lower left). The latter complication makes the ligation of the ductus hazardous. Recently, tracheal compression by the remaining pulmonary artery in an infant with agenesis of the lung was reported This mechanism may explain the cause of death early in life. In the adult, agenesis of the lung, unless complicated by a congenital cardiovascular anomaly or pulmonary disease, is compatible with a normal life

Pulmonary Arteriovenous Fistulas. A few years ago, the existence of pulmonary arteriovenous fistulas was unknown Since the advent of safe exploration of the lungs by means of angiocardiography, body section radiography, and fluoroscopic recognition of change

nosis during life in the unruptured state can be made by angiocardiography.

Associated Anomalies with Aortic Sinus Aneurysms. Angiocardiography provides the definitive diagnosis of aortic sinus aneurysm (Fig 6-78C, D). Generalized aneurysmal dilatation of the aortic sinoses was present in all but one of four cases, where only the right aortic sinus was involved. In the cases with coarctation of the aorta, the point of coarctation, the dilated brachiocephalic and collateral arterial branches, as well as the enlarged left ventricle were clearly outlined In contrast, in a case of *pseudocoarctation*, although there was an unusually dilated left subclavian artery, an apparent point of coarctation, and a dilated descending aorta, there was no collateral arterial circulation (Steinberg, 1958).

ANOMALIES OF THE LARGE VEINS

Anomalous Insertion of Pulmonary Veins. In 1949, *partial anomalous insertion* of the right pulmonary vein into the inferior vena cava was first diagnosed during life by angiocardiography and cardiac catheterization. Since then, recognition of *totally anomalous pulmonary drainage* into the right atrium and its tributaries has also become possible Diagnosis of these conditions is important, the reanastomosis of pulmonary veins into the proper atrium in specially selected cases may be lifesaving (Sepulveda et al.).

Figure 6-79A shows a classic angiocardiogram of a patient with a right pulmonary vein draining into the inferior vena cava. The crescentic broad vascular channels of the anomalous right pulmonary vein converging toward the cardiohepatic angle and inferior vena cava are clearly identified.

When anomalous pulmonary veins from the lungs or the whole left lung insert into the *left* innominate vein, a characteristic roentgen picture results (Fig. 6-79B, C). The abnormal mediastinal and hilar shadows have been likened to a "figure of eight," a "dumbbell silhouette," a "mediastinal mustache," and a "cottage loaf." On angiocardiography, the widened mediastinal and hilar shadows on the left are seen to be due to the dilated common pulmonary venous trunk (persistent left superior vena cava) inserting into the left innominate vein, while on the right side, they are due to the dilated superior vena cava, enlarged because of the increased blood flow from the *left innominate* vein. The patient whose roentgenograms are illustrated in Fig. 6-79B, C was mistakenly diagnosed as having a lymphoma.



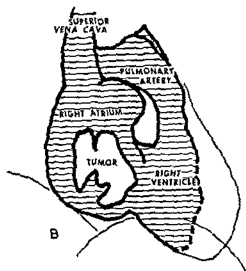


Fig. 6-81. A Right atrial myxoma producing tricuspid stenosis in a 35-year-old woman *Frontal* angiocardiogram showing a filling defect in right atrium and ventricle B. Tracing of (A). (*Courtesy of Dr. M S Belle.*)

Total Insertion of Pulmonary Veins into the Junction of the Superior Vena Cava and Right Atrium. This anomaly was found in a patient along with an associated atrial septal defect (this must exist for life). The conventional

in size of these lesions with respiratory maneuvers (Mueller and Valsalva), many cases have been recognized (Steinberg and McClenahan). Figure 6-78A shows the angiocardiogram of a patient with a pulmonary arteriovenous fistula. In the conventional roentgenogram, a nodular parenchymal shadow at the right base connected with the pulmonary artery and an efferent vessel (a pulmonary vein) at its lowest pole proceeded toward the left atrium. Angiocardiography (Fig. 6-78A) clearly visualized the lesion and localized the arteriovenous fistula in the posterior basilar segment of the right lower lobe.

AORTA

Unperforated Aortic Sinus Aneurysms. Aneurysms of the aortic sinuses (of Valsalva) are rare and are either congenital or acquired. The *acquired* types are chiefly due to syphilis or bacterial endocarditis. The *congenital* aneurysms are thought to be due to a developmental defect in either the aortopulmonary septum or the elastic tissue of the aortic sinuses. Diag-

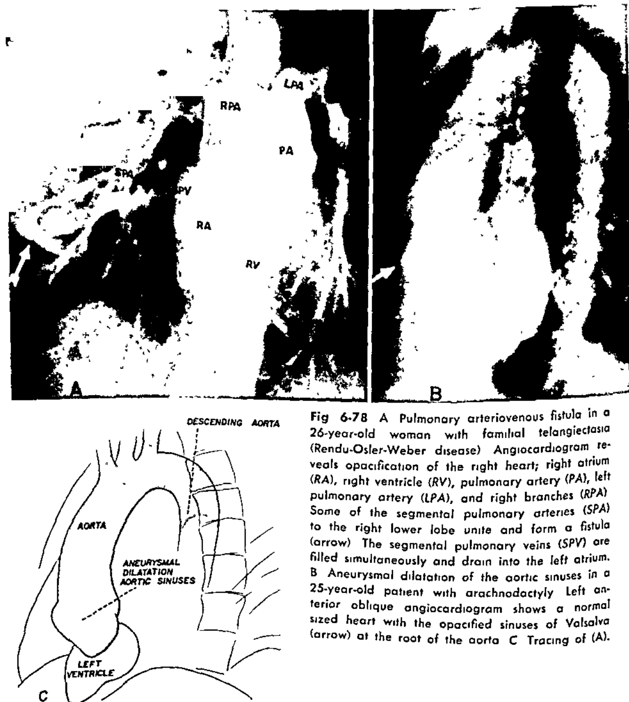


Fig 6-78 A Pulmonary arteriovenous fistula in a 26-year-old woman with familial telangiectasia (Rendu-Osler-Weber disease) Angiocardiogram reveals opacification of the right heart; right atrium (*RA*), right ventricle (*RV*), pulmonary artery (*PA*), left pulmonary artery (*LPA*), and right branches (*RPA*) Some of the segmental pulmonary arteries (*SPA*) to the right lower lobe unite and form a fistula (arrow) The segmental pulmonary veins (*SPV*) are filled simultaneously and drain into the left atrium. B Aneurysmal dilatation of the aortic sinuses in a 25-year-old patient with arachnodactyly Left anterior oblique angiocardiogram shows a normal sized heart with the opacified sinuses of Valsalva (arrow) at the root of the aorta C Tracing of (A).

12

Surgery of pulmonic stenosis with normal aortic root

C. GORDON SELL AND H. WILLIAM SCOTT, JR.

Pulmonic stenosis is one of the most common congenital cardiac malformations. It is frequently encountered in association with dextroposition of the aorta as a part of Fallot's tetralogy, but it also occurs in another large group of cases, in which the aorta has a normal origin from the left ventricle

Several classifications have been developed for this latter group of lesions None of them is entirely satisfactory but, for the purpose of clarity in this discussion, an anatomicoclinical grouping is suggested The true incidence of the various types of pulmonic stenosis is not accurately known Only in the last few years has it been recognized that many mild instances of pulmonic stenosis exist, for only recently has it become apparent that many patients with murmurs in the pulmonary area, which had been regarded as being functional, have in fact mild degrees of pulmonary stenosis Previously, it was thought that 60 per cent of patients with pulmonary stenosis and normal aortic root were cyanotic This estimate is inaccurate as it was based on surgical experiences which dealt naturally with the severe grades In patients studied by the authors by cardiac catheterization, the ratio of 5 acyanotic patients to 1 patient with cyanosis has been found The "dome-shaped" type of valvular stenosis is by far the most commonly encountered anatomic form of obstruction and is probably at least ten times more frequent than is infundibular stenosis or the combination of valvular and infundibular lesions (Fig. 6-82). Fortunately, from the surgical viewpoint, the "scarring" type of valvular stenosis with contraction of the valve ring is very rare.

ANATOMICOCLINICAL CLASSIFICATION OF PULMONIC STENOSIS WITH NORMAL AORTIC ROOT

A Pulmonic stenosis with intact ventricular and atrial septa (no shunts)
  1 Valvular
    a. "Dome-shaped" type
    b. "Scarring" type with contraction of annulus
  2 Infundibular
  3 Combined
B Pulmonic stenosis with intact ventricular septum and atrial diffusion (patent foramen ovale or interatrial septal defect)
  1 Valvular
  2 Infundibular
  3 Combined
C Stenosis of pulmonary arterial trunk and/or major branches with intact septa

INDICATIONS FOR SURGERY

Indications for surgical intervention in patients demonstrated to have pulmonic stenosis with normal aortic root fall, in the authors' opinion, into two categories—emergency and elective. Potts has pointed out that surgical relief of pulmonic stenosis may be required urgently as a lifesaving procedure in certain patients These are almost invariably young infants who are usually cyanotic and extremely dyspneic when first seen The evidence for the diagnosis of severe pulmonic stenosis rests on the presence of cardiomegaly, hepato-

in size of these lesions with respiratory maneuvers (Mueller and Valsalva), many cases have been recognized (Stemberg and McClenahan). Figure 6-78A shows the angiocardiogram of a patient with a pulmonary arteriovenous fistula. In the conventional roentgenogram, a nodular parenchymal shadow at the right base connected with the pulmonary artery and an efferent vessel (a pulmonary vein) at its lowest pole proceeded toward the left atrium Angiocardiography (Fig. 6-78A) clearly visualized the lesion and localized the arteriovenous fistula in the posterior basilar segment of the right lower lobe.

AORTA

Unperforated Aortic Sinus Aneurysms. Aneurysms of the aortic sinuses (of Valsalva) are rare and are either congenital or acquired. The *acquired* types are chiefly due to syphilis or bacterial endocarditis. The *congenital* aneurysms are thought to be due to a developmental defect in either the aortopulmonary septum or the elastic tissue of the aortic sinuses. Diag-

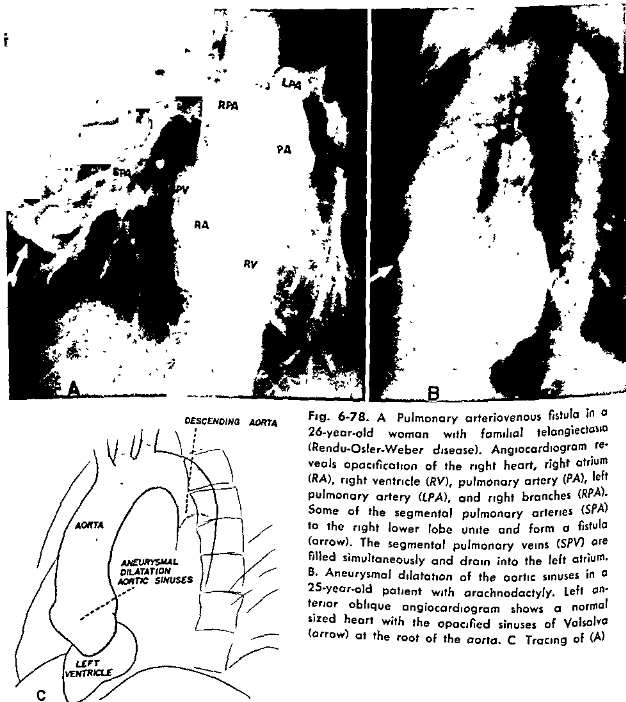


Fig. 6-78. A Pulmonary arteriovenous fistula in a 26-year-old woman with familial telangiectasia (Rendu-Osler-Weber disease). Angiocardiogram reveals opacification of the right heart, right atrium (RA), right ventricle (RV), pulmonary artery (PA), left pulmonary artery (LPA), and right branches (RPA). Some of the segmental pulmonary arteries (SPA) to the right lower lobe unite and form a fistula (arrow). The segmental pulmonary veins (SPV) are filled simultaneously and drain into the left atrium. B. Aneurysmal dilatation of the aortic sinuses in a 25-year-old patient with arachnodactyly. Left anterior oblique angiocardiogram shows a normal sized heart with the opacified sinuses of Valsalva (arrow) at the root of the aorta. C Tracing of (A)

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Surgery of pulmonic stenosis with normal aortic root

C. GORDON SELL AND H. WILLIAM SCOTT, JR.

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Fig. 6-80. A Bilateral superior vena cava in a 53-year-old woman Simultaneous injection of contrast material into both arms resulted in the opacification of right (*RSVC*) and left (*LSVC*) superior venae cavae. The coronary sinus (*CS*) entering the right atrium (*RA*) is well visualized. B. Cirsoid aneurysm of the right coronary artery (arrow) is demonstrated in the left anterior oblique angiocardiogram of an asymptomatic 7-year-old girl. An apical continuous murmur permitted the diagnosis of coronary arteriovenous fistula even though the site of anastomosis of the aneurysm could not be determined C. Left atrial myxoma in a 3-year-old child causing signs of mitral stenosis. Frontal angiocardiogram reveals a huge filling defect due to an atrial tumor. D. Tracing of (A).

fused cusps are divided to the annulus in a biradiate or triradiate fashion with small scissors (Fig 6-83) Reduction of body temperature to the range of 30 to 32°C and 3 or 4 min of cardiac inflow stasis are the chief requisites of the method

The Swan procedure has the advantage of direct visual control in division of the stenotic valve, and pressure measurements in patients treated in this manner have shown in most instances very satisfactory relief of the valvular obstruction, with a prompt reduction to normal in right ventricular pressures, a rise in pulmonary arterial pressures, and the elimination of any significant gradient across the valve.

In certain patients, however, the right ventricular pressure may remain elevated after completion of anatomically successful valvulotomy and returns to normal levels only after the passage of weeks or months. This is thought to be due to hypertrophy of the muscular wall of the right ventricular outflow tract which takes time to diminish

In the authors' opinion, the Swan operation of transpulmonary arterial valvulotomy under direct vision with hypothermia is the procedure of choice in the definitive relief of pulmonary valvular stenosis on an elective basis. In an initial series of 34 consecutive patients treated in this way by Swan and his associates, there were two operative deaths and excellent clinical results in the survivors. Thus far, in the authors' smaller series, the postoperative results have been equally good.

The Swan procedure has the disadvantages of being a more elaborate and time-consuming operation than Brock's method. While a median sternotomy can be used, Swan prefers bilateral anterior thoracotomy with transection of the sternum. Hypothermia with its inherent hazards and complications, including increased ventricular irritability, postoperative peripheral neuropathies, and subcutaneous fat necrosis, must in itself be listed as a disadvantage. Experience has shown, however, that these risks may be greatly reduced by not lowering body temperature below the range of 30 to 32°C This range permits interruption of circulation for a period of 4 to 5 min with reasonable safety This

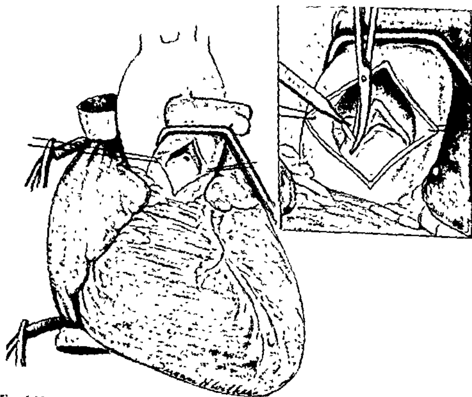


Fig 6-83. Direct exposure and division of stenotic valve by Swan's transpulmonary arterial method Hypothermia (30 to 32°C) and 3 to 4 min of circulatory stasis are used to permit valvulotomy under direct vision

chest roentgenogram suggested the diagnosis because of anomalous pulmonary vessel at the right base. Angiocardiography (Fig. 6-79D) confirmed the diagnosis by showing the newly recognized "jet sign," a filling defect at the site of insertion of the anomalous veins into the junction of the superior vena cava and right atrium. The filling defect is due to the turbulence created by the anomalous pulmonary venous blood flow.

Persistence of Left Superior Vena Cava. Recognition of persistence of the left superior vena cava has become possible with the advent of angiocardiography and cardiac catheterization. Simultaneous injection of Urokon through both arms shows the essential features of the anomaly (Fig 6-80A). Since publication of this case, persistent left superior vena cava associated with coarctation of the aorta has also been encountered.

ANOMALIES OF THE CORONARY ARTERIES

Coronary Arteriovenous Fistulas. Angiocardiography is not a reliable method of visualizing the coronary arteries. However, a cirsoid aneurysm of the coronary artery was visualized, and a continuous apical murmur at the apex of the heart permitted the diagnosis of a coronary arteriovenous fistula. Figure 6-71B shows the angiocardiogram of such a case.

ATRIAL MYXOMA

Atrial myxomas are of embryonal origin and may be classed as a congenital lesion. A significant advance in cardiac roentgenology was the recognition of intracavitary tumors during life by angiocardiography (Steinberg et al) Fortunately, primary tumors of the heart are rare. When they occur, they may produce bizarre and alarming symptoms, often with intractable heart failure that proves fatal. Four cases were diagnosed with the aid of angiocardiography (Figs. 6-80 and 6-81) which revealed filling defects

Reports of the successful removal of atrial tumors have been recorded in the literature Now that the diagnosis can be made by angiocardiography, further improvement in open-heart surgery will result in still more cures.

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Surgical treatment of ventricular septal defects

CONRAD R. LAM

It is a happy circumstance that a chapter on the practical aspects of the definitive surgical treatment of ventricular septal defects can be included in this volume. Until 1954, operations were available only to those patients whose septal defects formed a part of the tetralogy of Fallot and in whom there was diminished pulmonary circulation and right-to-left shunting with cyanosis. Operative treatment consisted of the creation of a systemic-pulmonary shunt (Blalock or Potts operation) or a cautious attack on the pulmonic stenosis, whether valvular or infundibular. Obviously, complete removal of the stenotic element would substitute one pathologic condition for another, i.e., there would be pulmonary hypertension instead of hypotension. Those patients in whom cardiac catheterization revealed an elevated pulmonary artery pressure were manifestly inoperable because cure was not possible without closure of the ventricular septal defect.

In 1954, Lillehei and his associates bypassed the heart by cross-circulation with a human donor and demonstrated that closure of ventricular septal defects under direct vision is feasible. Fortunately, the human donor as well as the heterologous (dog) lung and reservoir methods for bypassing the heart were soon replaced by a simple and inexpensive mechanical oxygenator of the bubble type. In the meantime, Kirklin and his associates had successfully used an oxygenator of the Gibbon type for the closure of ventricular septal defects.

Lillehei summarized the experience of his associates in 1957. They had operated on 154 patients with ventricular septal defects, with a mortality rate of 29 per cent. Obviously, the feasibility of this type of intracardiac surgical procedures is definitely established. However, it has become evident that there is ample opportunity for further refinements. First of all, the operative field is far from dry because, with the conventional bypass, only the venae cavae are occluded and the heart is allowed to beat, with the result that there is a continuous flow of blood from the coronary sinus into the right ventricle through the tricuspid valve. Also, there may be a serious backflow of blood from the aortic valve because of structural or functional insufficiency as a result of distortion. The motion of the beating heart is not conducive to the meticulous suturing indicated for the complete and permanent closure of the septal defect, which lies in such a critical area in proximity to the conduction system and the aortic valve. The answer to these problems lies in the principle of induced cardiac arrest.

In 1955, Lam and his associates reported on experiments in which the heart was stopped with the injection of potassium chloride into the left ventricle. With the brain protected by hypothermia, complicated operations were carried out in the atria and ventricles. Since no pump-oxygenator was available at that time, they had to depend on manual systole to expel the potassium salt from the coronary arteries, and ventricular fibrillation was a com-

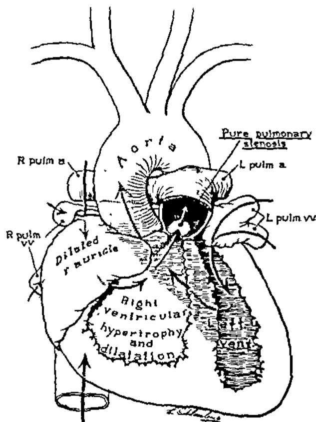


Fig. 6-82. Sketch of the most common type of pulmonic stenosis with normal aortic root (*Blalock and Kieffer. Ann. Surg.* 1950.)

megaly, ECG evidence of marked right ventricular hypertrophy and strain, with fluoroscopic and x-ray findings of right-sided cardiac enlargement accompanied by clear lung fields. The classic systolic murmur and thrill in the pulmonary area may be absent or very faintly detectable In these circumstances, cardiac catheterization and angiocardiography are frequently not feasible and the need for emergency surgical relief of the right ventricular obstruction is extremely urgent.

Indications for surgery on an elective basis for pulmonic stenosis with normal aortic root include patients with cyanosis and dyspnea who, in general, will be found to have right ventricular pressures of 70 mm Hg and over at rest and many of whom will show an ECG picture of right ventricular hypertrophy and strain with a mild to marked degree of cardiomegaly. At the present time, the authors do not feel that surgery is indicated in asymptomatic patients with right ventricular pressures in the range of 70 mm Hg or less with normal heart size and electrocardiographic findings. However, if as rarely occurs, a totally asymptomatic patient has a right ventricular pressure of 100 mm Hg or over, elective operation is indicated.

SURGICAL TREATMENT

Brock and Sellors (1948) independently recognized the need for a direct surgical attack on the site of obstruction in *valvular pulmonic stenosis.* They devised a transventricular approach whereby a simple valvulotome was passed via a small incision through the valve from below, splitting it transversely. The initial split was then dilated by sounds in an effort to extend the laceration to the annulus. Later Potts (1951) described his ingenious valvulotome with retractable blades and a dilator which functions on a similar principle. Many patients in both the cyanotic and acyanotic groups have been successfully relieved of obstructing valvular pulmonic stenosis by Brock's transventricular approach, both with the original rigid valvulotomes and by the use of Potts' instruments and their modifications. Included among the latter is the valvulotome with three retractable blades designed by Muller et al. Instead of splitting the valve in the Brock manner, Johnson has used a small guillotine knife and made several narrow bites in the valve after hooking it in the blades of the guillotine.

An approach to the stenotic valve by passing a valvulotome with retractable blades through a

of a diverticulum attached to the main pulmonary arterial trunk.

Postoperative catheterization studies in many patients with pulmonic stenosis treated by the various methods of blind instrumentation have shown that all too often a sizable gradient across the valve persists, indicating incomplete relief of the stenotic obstruction. These findings have emphasized the wisdom of monitoring pressures in the pulmonary artery and right ventricle during operation when closed techniques are used, in order to ensure adequate relief of the obstruction by repetitive instrumental splitting of the valve until the gradient is virtually eliminated.

Dissatisfaction with the results of closed methods led Swan (1953) to initiate the use of a method

by temporarily occluding the venae cavae. The

ceedingly important Postoperative hemorrhage must be watched for diligently and treated appropriately by blood replacement, additional protamine, and if necessary, exploration of the chest and pericardium The maintenance of a clear airway may be difficult, and the use of prophylactic tracheotomy in infants under the age of 1 year has much to commend it.

RESULTS

Sixty-two operations for the cure of ventricular septal defect have been carried out so far (1957) on 61 patients (one patient was operated on a second time because of early recurrence of the defect) There were 21 deaths in the entire series, giving a mortality rate of 34 per cent The relationship of age to mortality rate may be seen in Table 6-7. Slightly less than half of the infants under the age of 1 year survived In children over the age of 3 years, regardless of the other factors, the mortality rate was only 12 per cent

A significant factor has been the amount of experience of the surgical team with the technical aspects of the extracorporeal circulation procedure There were 5 deaths in the first 7 patients These patients received the low flows originally advocated, i e, 30 ml/kg/min. In the last 55 cases, this flow rate has been doubled, and out of 24 patients over the age of 3 years in this group, there has been only 1 death Even this death would have been prevented by the more generous dose of protamine sulfate now used routinely

In the analysis of the first 154 cases in his series, Lillehei found that the degree of pulmonary artery hypertension was an important factor in the recovery rate He divided the patients into two groups, those with severe pulmonary hypertension (70 per cent or more of aortic pressure) and those with moderate pulmonary hypertension (less than 70 per cent of aortic pressure). The mortality rate in 86 cases of the former group was 40 per cent, and in 68 cases with moderate pulmonary hypertension, the mortality rate was only 14.8 per cent An analysis of the author's series did not indicate a similar relationship. In fact, it turned out that the patients with the higher pulmonary artery pressures did statistically better (Table 6-8). It should be pointed out that the pressures in Lillehei's series were computed from aortic and pulmonary systolic pressures, while the pressures used for comparison in the author's series are *mean* arterial pressures

The important thing is whether the pulmonary hypertension is due primarily to flow or to resistance of the vascular bed of the lung Increased pulmonary flow is revealed by elevation of the pulmonary capillary wedge pressure,[1] x-ray evidence of increased pulmonary vascularity, and electrocardiographic evidence of left atrial and ventricular enlargement Resistance as the predominant factor is evidenced by pulmonary artery hypertension in the absence of parallel elevation of wedge pressure or pulmonary vein pressure, decreased pulmonary vascularity, and electrocardiographic indication of predominantly right heart enlargement. The fact that there were five survivals in the seven cases in which the pulmonary artery pressure was equal to that of the aorta was

TABLE 6-7 MORTALITY RATES WITH RESPECT TO AGE IN VENTRICULAR SEPTAL DEFECT CLOSURES

Age	*No of cases*	*Deaths*	*Mortality rate, %*
All cases	62	21	34
Under 1 year	15	8	53
Over 1 year	47	13	28
Over 2 years	32	6	19
Over 3 years	26	3	12
Over 3 years, pumped 50 ml kg/min	24	1	4

TABLE 6-8. RELATIONSHIP OF PULMONARY HYPERTENSION TO MORTALITY RATE

Degree of pulmonary hypertension	*No of cases*	*Deaths*	*Mortality rate, %*
Moderate (under 60 cm water mean pressure)	21	8	38
Severe (over 60 cm water mean pressure)	34	11	33
Extreme (balanced shunt)	7	2	29

[1] This point does not meet with general agreement *Editor.*

period is sufficient for the performance of an uncomplicated pulmonary valvulotomy but may be insufficient to deal safely with a more complicated lesion such as infundibular stenosis.

Perfusion of the coronary arteries with oxygenated blood during circulatory arrest with hypothermia has recently been used to enhance the safety of the technique by reducing the effects of myocardial hypoxia. With this modification and perhaps also with the addition of cerebral arterial perfusion, the safety of the Swan technique may be increased.

In the experience of the authors, the incidence of the murmur of pulmonic insufficiency has been higher after the Swan operation than following the Brock procedure However, follow-up studies of patients with such murmurs have led the authors to believe that they are hemodynamically unimportant. Whether mild pulmonary insufficiency has a higher incidence after triradiate incision of the stenotic valve than with bisection is as yet uncertain.

In the vast majority of cyanotic individuals with an atrial right-to-left shunt and pulmonic stenosis, there is a patent foramen ovale which is kept open by the elevated right atrial pressure. Following a successful pulmonary valvulotomy with reduction of pressures in the right side of the heart, the right-to-left shunt is automatically abolished, resulting in the functional closure of the foramen In a few cases, however, there is a large defect in the atrial septum, and successful valvulotomy has been followed by a large left-to-right shunt which has necessitated a second operation for closure of the atrial defect

A practical approach to the problem of atrial shunt with pulmonic stenosis at operation consists of inserting a finger into the right atrium after completing the valvulotomy in order to assess the status of the atrial septum by palpation. If only a small, slitlike valved foramen ovale is present, the authors feel that it can be safely ignored, on the other hand, if a larger atrial defect is present, it should be closed by one of the currently available methods.

The problem presented by the young infant with extremely tight pulmonic stenosis all too frequently constitutes a surgical emergency. In such instances, the authors have not used Swan's technique but have followed the method described by Potts, in which the heart is quickly exposed through a small left anterior thoracotomy and a cataract knife is passed through the stenotic valve via a stab wound in the right ventricle as a lifesaving measure. After creating a small opening in the valve in this way, the Potts valvulotome and dilator may be used to enlarge the opening. In the few cases treated in this way, the authors have felt that the use of the more elaborate and time-consuming technique of the direct visual procedure with hypothermia was unwarranted because of the precarious state of the infant.

Isolated infundibular pulmonic stenosis was first attacked surgically by Brock's closed transventricular punch-resection method. Glover, Kirklin, and a number of other surgeons in addition to Brock have reported satisfactory results in patients with this uncommon lesion treated by "blind" resection. The anatomic complexity of the lesion in infundibular stenosis, however, suggests the need for accurate and complete excision of the obstructing infundibular tissue under direct vision. This may be accomplished by the use of hypothermia and circulatory stasis, but the strict limitation of time permissible for open cardiac surgery with hypothermia alone is a serious objection to intraventricular surgery of any form using this technique Moreover, Warden et al. pointed out that a preoperatively unsuspected ventricu-

eral of their patients. Accordingly, it seems logical that surgical relief of infundibular stenosis with or without an associated valvular pulmonic stenosis should be accomplished by an open operation using *cardiopulmonary bypass* with a pump-oxygenator. Under these circumstances, the right ventricular outflow tract may be visualized in its entirety, the stenotic lesions dealt with accurately, and an associated ventricular septal defect, if present, may be closed

As experience with pump-oxygenators increases, the indications for the use of cardiopulmonary bypass with an extracorporeal circulation will certainly be extended. It is not unlikely that, in the near future, it will be advisable to carry out all types of intracardiac and valvular surgery under direct vision with the aid of a pump-oxygenator.

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Surgical treatment of transposition of the great arteries

THOMAS G. BAFFES

It is hardly likely that the surgical procedures used today for the correction of transposition of the great vessels will be anything more than intermediary operations However, they serve two important purposes. (1) they alleviate the symptoms to the extent that they avoid invalidism in the patient, and (2) they bring into sharp focus many physiologic and pathologic findings about transposition which might contribute to further progress in its correction The surgery of transposition, therefore, should be discussed in the light of these contributions.

PATHOLOGY OF TRANSPOSITIONS

Basically, transposition of the great vessels is the result of failure of the embryonic aorto-pulmonary septum to spiral, with the result that the aorta comes off the right ventricle and the pulmonary artery originates from the left ventricle As a result, the unoxygenated blood returning via the venae cavae is returned through the aorta to the periphery, while the oxygenated blood from the pulmonary veins is returned to the lungs by way of the pulmonary artery The systemic and pulmonic circulations are thereby completely isolated from one another—a situation incompatible with life, except for the fact that a certain amount of mixing of the two circulations occurs through an interventricular septal defect, an interatrial septal defect, a patent ductus arteriosus, or combinations thereof Furthermore, the congenital deformity often is more complex. Superimposed upon it may be any one of many familiar congenital deformities. Thus, transpositions may be found in conjunction with valvular stenoses of all types, infundibular stenosis, right aortic arch, coarctation of the aorta, dextrocardia, etc A study of the pathologic conditions found at autopsy in 75 cases of transposition was made in order to classify the types of transposition which might be encountered. Five groups were identified.

Transposition plus Shunt. Forty-six specimens (61.3 per cent of the cases studied) were transpositions having only interventricular septal defect, interatrial septal defect, patent ductus arteriosus, or combinations of these additional deformities. There was no obstruction to blood flow through the heart.

Transposition plus Coarctation of the Aorta. Eleven specimens (14 7 per cent of the cases studied) consisted of transposition in conjunction with infantile or adult coarctation of the aorta.

Transposition with Isolated Dextrocardia. One specimen (1.3 per cent of the cases studied) resembled in all details the simple transpositions in the first group, except that it was a mirror image of that type of heart.

Transposition with Pulmonary Stenosis. Twelve specimens (16 0 per cent of the cases studied) had transposition in conjunction with organic pulmonary valve stenosis, bicuspid pulmonary valve, or infundibular stenosis of the right ventricle.

Transposition with Tricuspid Stenosis. Five specimens (6.7 per cent of the cases studied) had tricuspid valve stenosis or atresia.

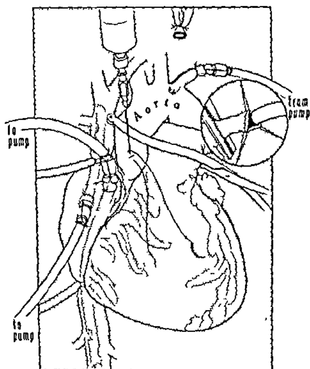


Fig. 6-84. Diagram of cannulations for bypassing the heart with the pump-oxygenator and method of inducing cardiac arrest by the injection of the cardioplegic drug, acetylcholine.

mon complication However, in a series of 20 animals, only one had refractory fibrillation Later, the authors began tests with *acetylcholine* as the cardioplegic drug and it was found excellent for the purpose In the meantime, Melrose demonstrated that *potassium citrate* is useful for inducing cardiac arrest, and this method has been applied clinically by Effler and his associates.

METHOD

Details of the technic which the author and his associates have used in the repair of interventricular septal defects have been presented in detail (1957), and only a summary will be included here.

The chest is opened through a transverse incision through the 3d interspace and the sternum After heparinization of the patient, the left subclavian artery and the venae cavae are cannulated (Fig. 6-84) and attached to the appropriate outflow and inflow tubes of the pump-oxygenator system. When a test with the pump running shows that the inflow and outflow are balanced, a noncrushing clamp is placed across the aorta (and also the pulmonary artery for reasons of convenience), and *acetylcholine in the amount of 10 mg per kilogram of body weight* is injected into the aorta proximal to the clamp. The drug enters the coronary arteries and promptly stops the heart. An incision is then made in the outflow tract of the right ventricle, and the defect is exposed. In a fair number of cases, it will be necessary to divide one or more papillary muscles, so that the septal tricuspid leaflet may be retracted better. The common type of high defect is shown in Fig. 6-85. Closure is effected by placing interrupted sutures which are tied over a pledget of Ivalon sponge No recurrence of the defect has been noted following this type of closure.

As soon as the intracardiac part of the operation has been completed, the heart is started by removing the aortic clamp. This permits the perfusion of oxygenated blood through the coronary arteries, and the acetylcholine is washed out. The blood which contains large amounts of the cardioplegic drug passes out of the coronary sinus, through the tricuspid valve, and into the open right ventricle, where it escapes during the closure of the incision into the right ventricle. As a rule, an excellent heart beat is present by the time the ventricular suture line is finished. The cannulas are then removed from the venae cavae and subclavian artery, and protamine sulfate solution is injected to neutralize the heparin. A few sutures are placed in the pericardium, and the chest is closed with drainage tubes in both thoracic cavities.

The postoperative care of patients who have had repair of interventricular septal defects is ex-



Fig. 6-85. Exposure of the ventricular septal defect and method of closure with sutures tied over a patch of Ivalon sponge Note that the sutures are passed through the fibrous tissue of the left ventricular side of the septum rather than the muscular tissue on the right side, to avoid conduction bundle injury.

years. In general, the patients had no postoperative cyanosis at rest and had only slight blueness of the lips and nail beds after exercise. *After operation, they also demonstrated* marked increase in exercise tolerance and visible increase in muscle mass of the thighs and calves. Those who had suffered from episodes of syncope, no longer had those attacks. Mental alertness was notably increased Those who *had hepatic enlargement and ascites before* operation had decrease in size of the liver and disappearance of the ascites.

probably because no cases of balanced shunt with marked pulmonary resistance and little or no flow were accepted for the operation.

There have been no late deaths or serious complications in the patients who have lived more than 2 days after the operation, with the exception of the one instance of early recurrence. The clinical improvement following the closure of the shunts has been remarkable. Weight gain in the undernourished children has been rapid. The cardiac status has promptly changed into a normal one. Normal activity has been tolerated within the first few weeks. A surprising dividend has been the rapid change of the radiologic picture of the heart toward one that is essentially normal.

SUMMARY

The repair of ventricular septal defects is a relatively safe surgical procedure, provided reasonable candidates for the operation are selected and the technical details of the operation are carefully managed. The poorest results are obtained in infants (under the age of 1 year) and in patients with high pulmonary arteriolar resistance. The best results are obtained in children above the age of 3 and in patients with high pulmonary artery flows.

Induced cardiac arrest with acetylcholine as the cardioplegic agent is a valuable adjunct during the cardiac bypass with the pump oxygenator.

PATHOLOGIC PHYSIOLOGY

Spontaneous closure of the ductus arteriosus probably occurs in the first 2 weeks following birth.[1] The exact involutional process is not entirely clear Barclay et al., in their studies on sheep, indicate that the ductus is functionally closed within a few minutes after initiation of pulmonary function Gross has stated that the variation of the insertion of the ductus away from an acute angle to a more obtuse one would tend to keep it patent. Kennedy and Clark have suggested that inadequate oxygenation of the blood promotes patency of the [illegible] Taussig suggests a lack of [illegible] ductus is accomplished by a membrane [illegible] the pulmonary end She suggests that such a membrane might rupture with rising systemic pressure and account for the appearance of signs of a patent ductus arteriosus in later childhood or adult life

Although the physiology and diagnostic features of patent ductus arteriosus are considered in detail in another section of this book (Part 1, Chaps. 1 and 2), there are certain features which are of concern to the surgeon in his approach to the problem. Usually, if a ductus is not closed within the first few months of life, it will probably remain patent, and in most cases surgery may be performed after 3 years of age The so-called *atypical ductus* in infancy, having only a systolic murmur, is a natural phenomenon resulting from the lack of elevation of systolic-diastolic pressure in the systemic system to promote flow during both systole and diastole With the raise in pressure, the continuous *machinery murmur* is then heard The size of the ductus varies in diameter from 0 5 to 1 cm and, in length, from practically a contiguous pulmonary artery and aorta to 1 to 1 2 cm in length Anatomically, a patent ductus may be classified into *cylindrical, funnel,* or *window* types Another important consideration is the early appearance of *pulmonary hypertension* with the large ductus and resultant bidirectional flow and reversal of flow This will be discussed below in more detail (pp 6–182).

The patent ductus arteriosus may be associated with other congenital anomalies. Pulmonary stenosis may be associated with a patent ductus arteriosus and account for a persistent murmur after correction of the ductus. The ductus may serve as a lifesaving measure in the presence of pulmonary atresia and in certain cases of transposition and truncus arteriosus Finally, a patent ductus may be present distal to a coarctation of the aorta, resulting in cyanotic lower extremities and noncyanotic upper extremities. Although most of the literature is concerned with treatment of patent ductus in children, there has been a gradual increase in experience with adults over the years, and this introduces an additional pathologic and surgical problem in that, in adults, the ductus is more friable and there are often associated degenerative changes both in the aorta and the ductus itself, making for increased hazard in its surgical treatment. Aneurysm of the pulmonary artery is associated with a patent ductus in a significant percentage of cases It usually is in the main pulmonary trunk Aneurysms of the ductus itself are rare and consist of dilatation of the aortic end of the ductus, with the pulmonary end being closed Graham has reported on this aspect.

INDICATIONS AND TECHNIQUE

There is general agreement that the actual existence of the lesion, patent ductus arteriosus, is indication for surgical intervention. The low mortality associated with operating on infants and children, particularly above 2 years of age, as contrasted with the increased mortality in adults, emphasizes the urgency of correcting this condition in childhood. Contraindications to surgery may be present in those patients in whom some other condition makes surgery extremely hazardous. Secondly, operation below 2 years of age probably should *not* be done, except in those cases in which there are progressive signs of deterioration and cardiac failure due to the presence of the ductus. Other contraindications would fall in that group in which the ductus is serving a function in association with other congenital anomalies and correction of the patent ductus without recognition of the underlying pathologic condition would result in disaster. Most surgeons agree that treatment of bacterial endocarditis should precede surgical division of the ductus. Finally, the presence of a so-called atypical ductus, or ductus with reversal of flow, may be

[1] See Part 1, Chap 2 *Editor*

It is apparent from this classification that all transpositions cannot be treated in the same manner. In the first three groups, it is possible to attempt to redirect the systemic and pulmonary circulations. In the last two groups, however, the basic difficulty consists of insufficient blood supply to the lung. These patients will respond to standard aortopulmonary or systemic-pulmonary anastomoses. Empirically, the pressure in the pulmonary artery has been utilized to decide which patients should have surgical redirection of the systemic and pulmonary circulations and which should be treated with the shunt operations. *Those whose pulmonary artery pressure is over 200 mm of water receive the former, those whose pulmonary artery pressure is less than 200 mm of water are treated with the latter.*

The problem of finding a suitable method for redirecting the systemic and pulmonary circulations has been a formidable one Four types of approach to the problem have been evolved (1) The earliest attempts consisted of methods for enlarging or creating interventricular or interatrial septal defects, combined with forced shifting of blood from one side of the heart to the other by means of vascular anastomoses. These methods, however, did not alleviate symptoms sufficiently. (2) Attempts were then made to divide the aorta and the pulmonary artery at their bases and transfer them to their correct ventricles. These methods generally did *not* transfer the coronary circulation, and thereby created conditions similar to congenital anomalous coronary arteries (3) A third approach to the problem utilized hypothermia or extracorporeal circulation to permit opening the right atrium and shifting the interatrial septum in such a way that the two circulations are properly redirected. None of these attempts has resulted in clinical success (4) The remaining approaches concentrated upon transplanting the venous return to the heart in such a way that the unoxygenated blood from the venae cavae was directed to the lungs and the oxygenated blood from the pulmonary veins was directed to the aorta. This problem has not been entirely solved, but transplantation of the right pulmonary veins and the inferior vena cava is now possible, rerouting approximately 60 per cent of the pulmonary and systemic circulations and greatly improving the peripheral oxygen saturation of the patient. Such a procedure is being used at the Children's Memorial Hospital in Chicago.

OPERATIVE PROCEDURE

A curved posterolateral incision is made through the right 5th intercostal space, and the right pulmonary artery, right main bronchus, right pulmonary veins, lateral aspect of the right atrium, and the inferior vena cava are dissected free. A curved coarctation clamp is applied to the lateral aspect of the inferior vena cava, in such a way that blood flow from the inferior vena cava into the right atrium is not impeded An incision is made in the excluded lip of the cava, and a homologous aortic graft is anastomosed to it. The right pulmonary artery and the right main bronchus are then occluded with umbilical tapes in order to prevent congestion of the right lung during the remaining maneuvers.

A coarctation clamp is applied to the base of the right pulmonary veins, allowing them to be severed from the left atrium with a common pedicle. The opposite end of the homologous aortic graft is then anastomosed to the left atrial stump of the right pulmonary veins. The distal end of the right pulmonary veins is anastomosed to the lateral aspect of the right atrium, part of its wall being excluded with a curved coarctation clamp for that purpose. The temporary umbilical tape ligatures are removed from the right pulmonary artery and the right main bronchus The right lung is aerated After the patient has had a few minutes to adjust to the new circulation, the flow of blood from the inferior vena cava through the aortic graft into the left atrium is made obligatory by placing a ligature around the base of the inferior vena cava at its point of entry into the right atrium. The pericardium is repaired, endothoracic drainage is provided, and the operative incision is closed.

RESULTS

Thirty-eight patients have been operated upon in this manner. Twenty-three survived the immediate postoperative period, an operative mortality of 39 4 per cent. Four patients died after leaving the hospital, of infection or pulmonary hypertension. The remaining 19 long-range survivors have shown very satisfactory clinical improvement From a preoperative peripheral oxygen saturation of 35 to 50 per cent, they have had increases in oxygenation amounting to 30 to 50 per cent Their postoperative peripheral oxygenation has ranged from 85 to 92 per cent of capacity

The youngest patient surviving this operation was 6 weeks of age. The oldest was 12

of Waterman et al. on the surgery of patent ductus arteriosus is important as it represents a composite of experience of 49 different collaborators, which in turn represents the work of even more surgeons. The report covered 4,448 operative cases, 552 being eliminated, leaving 3,896 reportable cases, of which 2,929 were performed on children and 967 on adults. The over-all mortality was 2.77 per cent. In the children's group it was 2.3 per cent, and in adults it rose to 5.5 per cent. There was very little difference in the mortality with ligation versus division.

If, however, one introduces the factor of pulmonary hypertension, then the total experience in this group of cases is not sufficient to reach an exact conclusion. It is recognized that, if the shunt reverses from a predominantly left-to-right flow, then the hazards of interruption of the ductus are increased. Ellis et al. advised *against closure* of the patent ductus in patients with sufficient pulmonary hypertension to produce an exclusively right-to-left shunt or one in which the right-to-left exceeds the left-to-right shunt. This was on the basis of a 50 per cent over-all mortality in 14 cases exhibiting such a level of hypertension. Gerbode et al. reported 11 patients with patent ductus and pulmonary hypertension of whom 10 were operated upon with complete closure, with one death occurring. Attempts to help solve this phase of the problem have been directed toward preoperative occlusion of the ductus by a balloon and temporary occlusion at the time of surgery with measurements of pulmonary artery pressure.

AORTOPULMONARY SEPTAL DEFECT

Aortic septal defect, aortopulmonary fistula, aortopulmonary defect, or aortopulmonary window are various terms applied to the failure of fusion of the aortic septum dividing the pulmonary artery and aorta. Although this is an extremely rare condition, it is of great importance because of its confusion with a patent ductus, which is so easily correctible surgically, as contrasted to this lesion which is far more difficult to treat. The development of this defect and its medical aspects, together with the diagnostic features, are included in other chapters.[3] In general, however, the clinical appearance of these patients is very much the same as that of patients with a patent ductus, and the final diagnosis is probably best made by *retrograde aortography* or actual placement of the *cardiac catheter* through the defect, from the pulmonary artery into the aorta. This condition, of course, may also be confused with other causes of continuous murmur in this area, namely, rupture of an aneurysm of a sinus of Valsalva into the right atrium or ventricle or rupture of an aneurysm of the aorta into the pulmonary artery or into the great veins, or finally an anomalous coronary artery draining into a cardiac chamber.

Variations in the anatomic characteristics of the aortopulmonary septal defect run from a truncus arteriosus (in which there is no septum between the pulmonary artery and the aorta), to a high interventricular septal defect, to an actual aortopulmonary window or defect (in which there is fusion of the septum below the defect, just at the origin of the aorta and pulmonary artery). The defect varies in size from 1 cm or less up to 6 cm, which was the size of one of the cases treated by the authors. The literature has been reviewed by Davis and Cooley. According to the latter, Hektoen (1900) reported the first case in American literature, and at the time of Cooley's publication (1957), 25 more cases had been recorded.

Gross apparently accomplished the first successful surgical approach to the problem of aortopulmonary septal defect. In 1948, he ligated such a defect with a tape ligature, and the patient survived with the defect closed. The next method of treatment parallels the development of surgical treatment of patent ductus, namely, division of the communication, with suture of the sectioned communication. One great difference, however, in the comparison of these two lesions, in so far as this surgical approach is concerned, is that, in the aortopulmonary window, the posterior wall is extremely thin and easily entered during dissection. Also, it may be difficult to get enough tissue on either side without compromising one or the other vessels.

Successful cases have been reported by Fletcher, using division and suture, and Davis

[3] See Chaps. 2 and 3. *Editor*

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Surgical treatment of patent ductus arteriosus and aortopulmonic defects

WILLIAM S. DYE AND ORMAND C. JULIAN

PATENT DUCTUS ARTERIOSUS

The surgical correction of a patent ductus arteriosus has become a standard procedure throughout the world. The development of this procedure constitutes one of the early chapters in the history of surgery for cardiac and extracardiac lesions. Historically, the early studies centered around the successful ligation of a patent ductus, with subsequent development of division and suture of the patent ductus The most recent studies have been directed toward the problem of the patent ductus associated with pulmonary hypertension

Munro (1907) first suggested ligation of the ductus arteriosus. Graybiel et al (1938) reported one of the first attempts to ligate a patent ductus. This was in a patient with bacterial endocarditis, and death occurred on the fourth postoperative day. Gross and Hubbard (1939) reported the first successful ligation of a patent ductus arteriosus In the same year, Gross reported again a summary of 4 surgically treated cases, and later (1940) reported his experience with 10 cases Additional successful cases were reported by Jones et al (1940) Johnson et al (1942) reported 7 cases and outlined the hazard of the posterior wall dissection They reviewed a death from hemorrhage in 1 case. They suggested more extensive dissection of the aorta and intrapericardial exposure of the pulmonary artery, if needed. Touroff in the same year described his experiences with the infected patent ductus arteriosus. The question of incomplete closure or subsequent recannulization following ligation of a ductus arose, and Gross (1944) reported, in addition to 14 cases treated by ligation, 14 subsequent cases with complete division, making a total of 28 cases in whom recannulization took place. Blalock had reported good success with simple ligation, however, using double ligation and transfixion.

Touroff had previously divided the ductus (1942), although it was not deliberate. This was done in a case of infected patent ductus, and the division was done during control of an inadvertent tear Jones (1947) reported 61 cases, 53 ligated and 8 divided In the ligated cases, 5 had a return of the murmur immediately and 5 subsequently. In the 8 cases, in which the ductus was divided, 7 survived with no recurrences of the murmur. In the same year, Gross reported further experiences with division of the ductus, and at that time reported 90 cases with 2 deaths. Potts (1948) first reported a new clamp for surgical division of the ductus, and his modification of Gross' technique for division, utilizing the multiple-tooth ductus clamp that has been widely used subsequently. During the first 10 years of development of surgery of patent ductus arteriosus, it became commonplace for surgeons over the country to approach the problem, and the trend was definitely away from multiple ligation to division of the ductus.

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The technique used in the authors' experience is based on the work of Gross and modifications by Potts and, in certain complicated cases, follows the suggestions of Conklin and Watkins, Jones, and Crafoord. Surgical exposure is through a posterolateral incision, and entrance to the thoracic cavity is through the 4th interspace. The authors are impressed by the increased safety of using the *posterolateral incision* as contrasted to the anterior submammary incision.

Following retraction of the lung anteriorly, the parietal pleura is incised over the anterolateral aspect of the aorta. The vagus nerve is immediately identified and dissected free and retracted. In most of the authors' cases the aorta is dissected free just distal to the subclavian artery, so that the posterior aspect is completely dissected, and cord tapes are placed superiorly and inferiorly to the ductus.

The vagus nerve is identified at the point where the laryngeal nerve comes off and the recurrent laryngeal nerve is exposed as the inferior aspect of the ductus is dissected Reflection of the pocket or lappet of pericardium on the anterior aspect of the ductus is accomplished by sharp dissection, as emphasized by Potts Section of the fibrous and areolar tissues above and below the ductus is also accomplished by sharp dissection Retraction of the aorta anteriorly may facilitate some of the dissection along the posterior aspect of the ductus, since it is in this area that blunt dissection by curved instruments may result in disaster, with tearing of the ductus. Superiorly, there is a firm fibrous attachment which has been labeled the *ligament of Gross* A ductus which often appears quite short at first may, after the completed dissection, be of adequate length for routine clamping and division Following the isolation of the ductus, angled ductus clamps, as designed by Potts, are applied to the pulmonary and aortic side It is important to place the clamp as close to and encroaching on the wall of the pulmonary artery and the aorta as possible to provide adequate length between the clamps for division and suture Two clamps may be used on either side In the majority of cases, the authors have used the single clamp on each side and have found it satisfactory. Usually the aortic stump is closed first. Sutures are accomplished with a running 5-0 Deknatel suture. Following release of the aortic clamp, the bleeding is controlled by pressure, and suture of the pulmonary stump is accomplished in a similar fashion The pleura is left open posteriorly in the majority of cases. The chest is closed with water seal drainage, even in children.

The foregoing technique may be applied to most cases of patent ductus arteriosus. In certain unusual circumstances, other modifications of the technique may be used. In the event of severe hemorrhage from a torn patent ductus, previous dissection of the aorta, as described above, facilitates the immediate cross-clamping of the aorta, as previously described by Crafoord. A ductus clamp, placed on the proximal pulmonary side, controls the hemorrhage and facilitates closure of the rent in the aorta. This method may be used particularly in adults with a very short wide ductus as a method of choice, although the use of hypothermia as an adjunct is recommended. However, in one adult case, as an emergency, the aorta was clamped without hypothermia to control hemorrhage, and cross-clamping of the aorta for 50 min resulted in no undue complications. Another method in the short ductus is the use of the Potts-Smith aortic clamp, as described by Conklin and Watkins and Potts This clamp, by virtue of its partially occluding the lateral wall of the aorta provides more length of the ductus and facilitates suture and division of the ductus at its entrance into the aorta without completely occluding the flow through the aorta itself. Finally, although this method should never be used as one of choice, simple ligation with the addition of suture ligatures may be employed. The use of simple ligature, such as an umbilical tape or heavy silk, probably results in a fairly significant incidence of recannulization and also, in the wider ductus, carries a great hazard of cutting through the wall of the ductus. Recently, partial occlusion of the ductus with subsequent reentry of the chest and complete division has been carried out in certain cases of atypical patent ductus with pulmonary hypertension in order to avoid the results of sudden occlusion of the patent ductus in these cases.

RESULTS

The over-all good results and low mortality associated with division of a patent ductus arteriosus, particularly in children, leaves no doubt in most physicians' minds of the feasibility and advisability of this procedure. The results in a large series, in children, show a consistent low mortality associated with the procedure, and in most cases it is less than 1 per cent Since there is no question about the ultimate results of an uncorrected patent ductus of any size, recommendation for surgical treatment of the condition in childhood seems without question. This applies, of course, to the so-called *typical patent ductus*. The report

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Hypothermia and heart-lung apparatus

Hypothermia

F. JOHN LEWIS

Experimental Studies on Cardiopulmonary Bypass

KARL E. KARLSON AND
JACKSON H. STUCKEY

Clinical Studies on Open-heart Surgery and Cardiac Bypass

RALPH A. DETERLING, JR.

HYPOTHERMIA

Hypothermia finds application in heart surgery because it reduces metabolic rate When employed during anesthesia, it slows all life processes, causing profound depression as low temperatures are reached With sufficient cooling, the heart beat stops and metabolism almost ceases, yet recovery is still possible, even from near-freezing temperatures The surgeon who employs hypothermia may, theoretically at least, simply select the degree of metabolic slowing that he needs and then lower the temperature to the proper level All degrees of cooling, down to near freezing, have been used clinically The effect of hypothermia is striking, and its use has exerted considerable impact on the development of cardiac surgery. There are still technical difficulties and hazards associated with profound cooling, nonetheless, which limit its full use at present

HISTORY

A start in the use of hypothermia for cardiac surgery was made by McQuiston and by Potts, who advocated mild cooling of infants undergoing surgery for cyanotic heart disease, but the big advance was made by Bigelow and Boerema, independently, in 1950, who demonstrated experimentally that open-heart surgery could be performed under hypothermia and with temporary cardiac inflow interruption Clinical application of this technique began in 1952 (Lewis and Taufic), and shortly thereafter the method was widely employed to repair atrial septal defects and then isolated pulmonary stenosis However, the time allowed for open-heart repair was limited with this simple technique to 8 to 10 min at temperatures that were safely attained (28 to 30°C), and this was not enough for more complicated repairs

Stimulated by the achievements obtained with hypothermia, work with extracorporeal circulation, which dated back to Gibbon's studies in the 1930s, went on at an accelerated pace, soon *pump-oxygenators* were being employed at several medical centers for open-

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The technique used in the authors' experience is based on the work of Gross and modifications by Potts and, in certain complicated cases, follows the suggestions of Conklin and Watkins, Jones, and Crafoord. Surgical exposure is through a posterolateral incision, and entrance to the thoracic cavity is through the 4th interspace. The authors are impressed by the increased safety of using the *posterolateral incision* as contrasted to the anterior submammary incision.

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tory mixture of 5 per cent carbon dioxide and 95 per cent oxygen to keep the blood pH at a relatively constant level during moderate hypothermia, and Edmark recently has advocated intravenous hydrochloric acid with the same objective in mind

Antifibrillatory drugs might offer a solution, and many drugs have been tested Of the well-known drugs, only *quinidine* has significant protective action; one antihistaminic drug, *antazoline*, also appears to have protective action (Angelakos). Prostigmine, injected in high concentration into the coronary circulation (by injecting it into the ascending aorta), is also helpful (Montgomery et al., 1954) and local anesthesia of the SA node by injection with Nococain may help (Riberi et al.). Other drugs have been credited with a protective action, but the toxic effects easily outweigh the potential protective effects in most cases. Quinidine and antazoline are probably the best, but they have found very little practical application.

Cardiac function and metabolism are affected by hypothermia, of course, whether or not fibrillation occurs With deep or prolonged cooling, the heart will finally fail, but with only moderate cooling of short duration it may actually increase in efficiency (Badeer). The heart functions quite well at temperatures above 20°C for relatively short periods. Coronary arteriovenous difference remains normal, suggesting that cardiac hypoxia does not develop. A number of investigators have identified damaging effects of hypothermia, however. Edwards et al. found, in contrast to Badeer, that the mechanical efficiency is decreased with cooling Cardiac failure and ischemic damage have been found in other studies, most of which were complicated by the addition of temporary circulatory occlusion or a surgical incision.

Coronary blood flow decreases during cooling as a logical consequence of several changes produced by cooling: decreased cardiac output, fall in arterial blood pressure, decreased heart rate, increased blood viscosity, and a relative lengthening of ventricular systole. Reduced coronary arterial resistance produced by the cold tends to oppose these other changes and promote flow, but still coronary flow decreases Efforts to increase coronary flow may fail. If the heart rate is artificially increased, for example, coronary flow will be even further reduced because the diastolic filling period, essential to coronary flow, is shortened.

Electrocardiographic changes during hypothermia are striking. All the time intervals of the tracing are lengthened as temperature falls, and the ST segment soon becomes elevated. This elevation has been cited as evidence that the muscle is anoxic (Lange et al.), but it could merely indicate that the heart carries an electric potential from one beat to the next without complete electrical recovery (Hoff and Geddes). Atrial fibrillation occurs commonly in man at temperatures of about 30°C, and complete heart block with idioventricular rhythm appears at about 15°C.

Peripheral Vascular Physiology. In hypothermia, as in other states where profound changes in cardiovascular function take place, such as shock, the question arises as to whether the principal change is in the heart or in the small vessels. Both are affected in hypothermia, but it is likely that small-vessel changes are the most important. If flow could be maintained through small blood vessels, even at a very slow rate, hypothermia would be better tolerated than it is. As matters stand, flow is inadequate, for several reasons, and tissues are poorly oxygenated in consequence. Peripheral vascular resistance increases, partly because of the increased blood viscosity, caused to some extent by the elevated concentration of blood cells. The increased resistance is also due to small-vessel constriction, which may not occur uniformly in various parts of the body. Thus, through poorly coordinated distribution, vital areas may lose their blood flow. Furthermore, a failure in coordination may be evident between small arteries and small veins if they do not constrict and relax simultaneously during cooling and rewarming. Haddy, for example, in studies conducted with the dog's foreleg, found that venous constriction persists longer than arterial constriction during rewarming, resulting in an increased capillary pressure which may lead to local loss of fluid. These observations may provide an explanation for the loss of plasma that occurs during hypothermia

Blood "sludging" during cooling provides another explanation for the increased vascular resistance. Red cells in the small vessels clump together in aggregates when temperature falls (Gelin and Lofstrom). These aggregates move sluggishly and finally they may actually occlude

using ligation. In Davis' case, a persistent murmur was thought to be due to the remaining dilated pulmonary artery. Hypothermia was added during repair of experimental defects via the pulmonary artery by Shumway and Lewis. These were defects created after the method of Scott and Sabiston, although these authors divided the communication and sutured the cut ends, and reported one successful case (1953). Cooley et al. (1956) reported three cases in which division and suture were done under hypothermia in one and division-suture using cardiopulmonary bypass in two. All three patients survived It was their feeling that the method of choice for repair of this defect was *a temporary cardiopulmonary bypass with induced cardiac arrest.* Scott stated they had operated on two more cases, with one death. The authors' experience included two cases treated by two different methods.

The first patient was a 6-year-old boy who had a 1-cm communication between the aorta and pulmonary artery and who was treated by division and suture, using hypothermia. In this case, considerable difficulty was encountered because of hemorrhage secondary to the dissection of the posterior aspect of the lesion. Inflow occlusion was necessary while the hemorrhage was controlled and the defects were sutured on both vessels. The second case was a large aortopulmonary septal defect measuring approximately 6 cm in diameter. This patient was a 28-year-old, white woman with severe pulmonary hypertension She was operated upon using a temporary cardiopulmonary bypass. The technical aspects of the repair of this large defect were greatly facilitated by the use of a cardiac bypass, and dissection was accomplished with ease. It was necessary, however, to use an Ivalon patch to make up for deficiency on the pulmonary side, and following completion of the procedure, hemorrhage from this side resulted in death.

The necessity for repair of this defect comes from the likelihood of development of pulmonary hypertension, the constant left heart strain, and the possibility of endocarditis.

So far, limited experience with repair indicates that open repair using cardiopulmonary bypass is the method of choice.

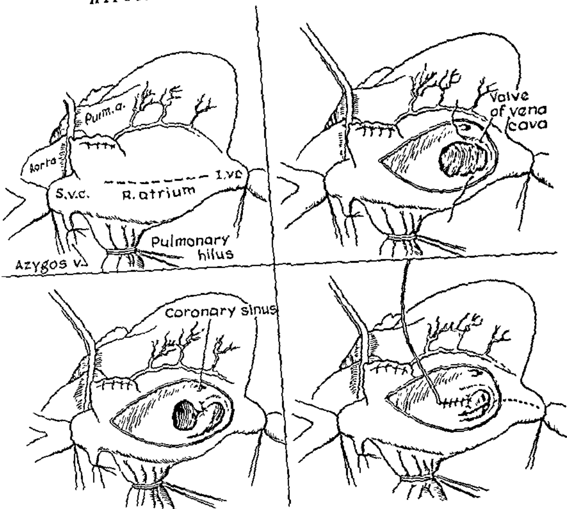


Fig. 6-87. Steps in the repair of an atrial septal defect with hypothermia and temporary cardiac inflow occlusion. (From Lewis.)

which have an *anomalous pulmonary venous drainage.* These are both defects that can be closed with a simple continuous stitch plus a few reinforcing stitches. Hypothermia provides enough operating time.

A few years ago the author and his associates reported on the repair of 63 atrial septal defects with this technique. Follow-up catheterization showed that the repair had been lasting in most cases. Swan has done as well with this technique, and many other surgeons have used it for these relatively simple, uncomplicated defects. Even today, when a number of functioning pump-oxygenators may be found in every city, the use of hypothermia alone is justified for these defects. Its use *is not justified* for defects of the ostium primum type, *atrioventricular canal defects,* or *ventricular septal defects.* Since preoperative diagnosis is not always reliable in differentiating these various defects from simple atrial septal defects, *most surgeons* doing open-heart surgery repair all atrial septal defects with extracorporeal bypass.

Pulmonary stenosis with a normal outflow tract is another lesion for which hypothermia with inflow occlusion has been successfully used. Again preoperative diagnosis must be accurate, for the technique is not satisfactory for infundibular stenosis or for combined lesions. The open technique with hypothermia, developed by Swan, was a distinct advance over blind transventricular operations, as demonstrated by its more successful relief of the pressure gradient across the valve. Sufficient open operating time is provided so that the fused valve cusps can be carefully divided under direct vision. In fact, Lam has advo-

heart operations, and a little later these machines were to be found in hospitals around the world. Expectations for the pump-oxygenators seemed now to be almost achieved. Certainly, they permitted much to be accomplished and extended greatly the range of intracardiac surgery. Hypothermia alone for open-heart operations had been a sort of stopgap while surgeons waited for the development of extracorporeal circulation. With extracorporeal circulation established, hypothermia assumed a minor role or was left no role at all.

Still, the idea of using hypothermia in combination with extracorporeal circulation appealed to many surgeons. This combination had been studied experimentally by Gollan et al. (1952, 1959) for some time, and it was logical to try hypothermia by means of blood cooling when some of the problems associated with extracorporeal circulation began to be clearly recognized. At normothermia, a high, almost normal, blood flow was required of the machine in order to avoid serious metabolic acidosis, and this high blood flow was difficult to achieve without blood damage, emboli, and protein denaturation. Bypass might be easier if metabolic processes were slowed by cooling

Thus, in the early 1960s, some combination of extracorporeal circulation and hypothermia is a favorite means of performing open-heart surgery; various degrees of hypothermia, from mild to profound, have been used These combined systems, by no means ideal as yet, have provided some advantages over earlier techniques, and there is hope of further improvement

PHYSIOLOGY

If a patient is cooled while anesthetized sufficiently to prevent shivering, metabolic rate, pulse rate, and respiratory rate decrease. If the temperature is lowered enough, respiration stops, and at a still lower temperature (usually below 15°C) the heart stops At 28°C, oxygen consumption is only 55 per cent of normal; at 20°C, it falls to 20 per cent of normal (Bigelow et al., 1950). Regularly, in the principal organs and body systems, there is a pattern of reduced metabolic rate and increased tolerance to ischemia during hypothermia. The cardiovascular system, which is of particular concern in this presentation, follows the general pattern; furthermore, it is the critical system, because during profound or prolonged hypothermia, circulatory failure is the commonest cause of death. If circulation could be maintained adequately through all tissues, warm-blooded animals might behave like hibernators and hypothermia would be safer and more useful than it is at present.

Cardiac Physiology. The cardiovascular physiologic alterations are both central and peripheral. The most dramatic central cardiac alteration that may occur during hypothermia—*ventricular fibrillation*—has attracted great interest, but its cause is still not well understood and there are no uniformly successful ways to prevent it. Cardiac surgeons have learned to get along with ventricular fibrillation in operations employing hypothermia deep enough to cause it. The circulation is maintained with extracorporeal bypass during the danger period before and after fibrillation, and a regular heart beat is restored during rewarming by means of *electrical defibrillation*. Nonetheless, attempts to understand and prevent ventricular fibrillation are important, for these studies could strengthen the further development of hypothermia techniques.

Ventricular fibrillation rarely occurs above 25°C in closed-chest experiments, but it is likely to occur below 20°C. If the ventricles are traumatized during preparations for an open intracardiac operation, fibrillation is likely to occur even at temperatures of 28 to 30°C This arrhythmia will occur readily in the dog, perhaps not quite so easily in man, and not at all in rats or hamsters. Obviously hypothermia predisposes to some alteration of cardiac excitability, and several detailed explanations have been proposed Though recognizing that the whole matter is not clear, Hoffman points out that cooling produces changes in electrical activity that predispose to multiple firing, local blocks, or reentry. Action potential set off repetitively may fail to enter the specialized conduction system and may start a ventricular fibrillation instead A good understanding of this mechanism may require studies of single muscle fibers.

To avoid ventricular fibrillation, surgeons have employed the practical solution of simply avoiding too low temperatures. If care is used in handling the heart, temperatures of 28 to 30°C are relatively safe. Respiratory control to avoid alkalosis or rapid shifts in pH also lowers the propensity to ventricular fibrillation. The author and his associates have used a respira-

be used with another, somewhat simpler type of extracorporeal circulation in which the patient's lungs provide the oxygenation while pumps substitute for the heart (Drew and Anderson, Shields and Lewis).

A catheter placed in the right atrium drains blood by gravity into a small reservoir, from which it is pumped into the pulmonary artery, thus substituting for the right side of the heart. The left heart is bypassed similarly, with a catheter draining blood from the left atrium into a small reservoir, from which it is pumped by way of a blood heat exchanger into the femoral artery (Figs 6-88 and 6-89) This system for open-heart surgery has advantages over a pump-oxygenator because a much smaller volume of extracorporeal blood is required (only 1,000 ml) and because the patient's lungs, rather than a machine, are used for oxygenation On the other hand, cannulation is more difficult, and circulation must be stopped to operate in some chambers of the heart. Since the atria are used for blood collection, they cannot be opened for surgery while the pumps are running This pertains especially to the left atrium; the right atrium may be bypassed by simply inserting catheters into the superior and inferior venae cavae. Similarly, the mitral valve and most parts of the ventricular septum cannot be exposed while the circulation is running. This problem is managed by making hypothermia part of the technique. With a blood heat exchanger in the blood line, the patient is cooled to any desirable temperature, and circulation may then be completely stopped to obtain a dry heart for repair. Though this provides the opportunity to operate in all parts of the heart, the permissible operating time is limited to approximately 30 to 45 min when central body temperatures are around 15°C.

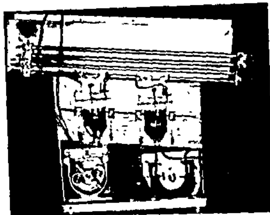


Fig. 6-89. Apparatus used for hypothermia with autogenous oxygenation. The blood heat exchanger is placed horizontally at the top.

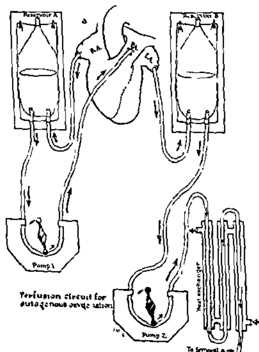


Fig. 6-88. Diagram showing the blood circuit for hypothermia with autogenous oxygenation. The pumps, which are semiautomatic in operation, maintain a constant level of blood in the small disposable reservoirs.

At present, it would not seem wise to use this technique for all types of open-heart surgery. The author and his associates prefer it to the pump-oxygenator for *atrial septal defects* and *isolated ventricular septal defects*, and possibly for *pulmonary valve disease*. They have also operated upon the aortic valve and the mitral valve but the operations were relatively brief. If replacement of any significant portion of the valve is contemplated, a pump-oxygenator provides a better operative technique at the present time.

EXPERIMENTAL STUDIES ON CARDIOPULMONARY BYPASS

A number of problems are common to both partial and total cardiopulmonary bypass. Some of these are the effect of pump-oxygenators on blood elements, effect of heparinization on coagulation factors and tissues, and the use of various anticoagulants for perfusion.

the lumen of small vessels. Flow stops in some of the vessels, and the aggregates of red cells become small thrombi. An observer derives the impression that measures preventing this sludging would be enormously helpful during hypothermia.

Hypothermia is an abnormal state, and the adverse changes that it produces, especially if the hypothermia is prolonged or profound, limit its present use in cardiac surgery. With knowledge that could lead to better control, more extensive use of hypothermia would be justified, but even now, it has found valuable application in cardiac surgery.

CLINICAL APPLICATIONS

Open-heart Surgery with Surface Cooling and Cardiac-inflow Interruption. Surface cooling with temporary cardiac-inflow interruption is technically the simplest way of performing open-heart surgery. Under anesthesia deep enough to suppress shivering, the patient is cooled by refrigerating blankets or an ice-water bath (Fig 6-86) Active cooling is discontinued a few degrees above the desired level, the temperature will drift down—usually to 28 to 30°C—as the operation proceeds After preparations have been completed, both venae cavae are occluded to stop cardiac inflow, cardiac outflow is occluded by clamping the pulmonary artery and aorta, and the heart chamber, usually the right atrium or pulmonary artery, is opened to expose the defect in a dry, relatively quiet field (Fig. 6-87). When the repair has been completed, the heart is filled with saline solution or blood to wash out air, and the cardiac wound is closed with a suitable clamp as circulation is resumed by releasing the inflow and outflow occlusions Rewarming is done by heating the body surface, usually with the same type of apparatus that was used for cooling.

Surgeons using this technique discovered that *body temperatures below 25°C were dangerous; ventricular fibrillation* was likely to occur and, even if it did not, cardiac action would be weak following the repair. They learned to get along with temperatures of 28 to 30°C, which allowed a maximum of only 8 to 10 min of open operating time; with this limitation, only relatively simple intracardiac operations could be attempted. Atrial septal defects of the *foramen ovale* type are suitable, as are most of the *high atrial septal defects,*

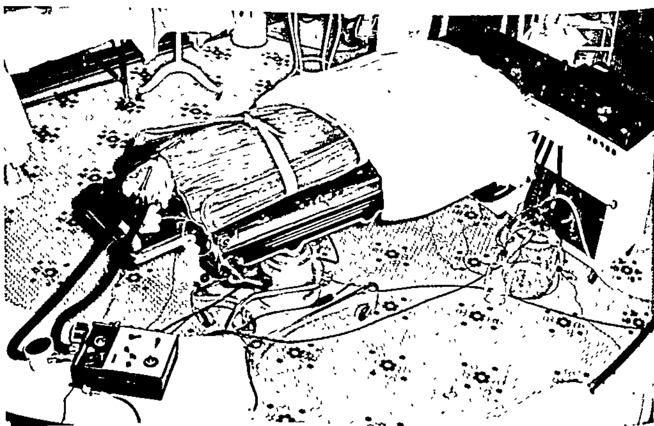


Fig. 6-86. The anesthetized and intubated patient is wrapped in the refrigerating blanket and a respirator is attached.

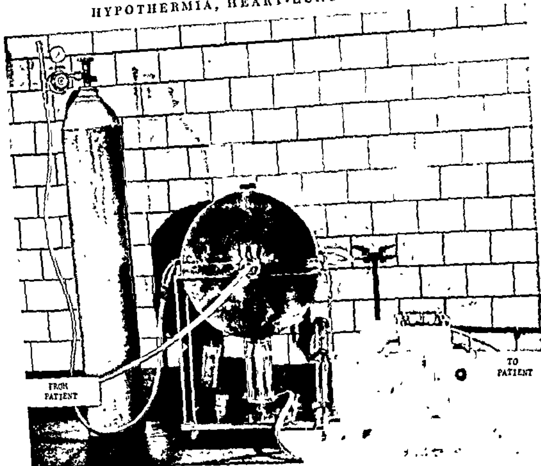


Fig. 6-90. Pump-oxygenator as used at Downstate Medical Center. Venous blood drains by gravity to the hollow central shaft of the oxygenator, from which it flows as a film onto the rotating stainless steel disks The blood is oxygenated in an atmosphere of 95 per cent oxygen and 5 per cent carbon dioxide during the filming process, courses through two bubble traps, and then is returned to the arterial side of the patient by an occlusive roller pump.

PATHOLOGIC CHANGES IN TISSUES FOLLOWING PERFUSION

One of the most important problems associated with perfusion, particularly prolonged partial perfusion, is the *hematuria* that has developed in all cases after the patient has been on partial cardiopulmonary bypass for 1 hr or longer A question arises concerning the possibility that this is the result of *infarcts* A review was made of the pathologic changes found in 20 dogs at various periods after total cardiopulmonary bypass (Kottmeier et al.) in an attempt to determine if associated histologic changes were present. In those animals which were sacrificed within 24 hr following perfusion, embolic material was found in the renal arterioles, after 24 hr, this material was not evident When stained with hematoxylin-eosin, this material has a purple-gray color and has been interpreted as representing *fibrin*. This material was found when antifoam had been used in the oxygenator and also when it had not been used. A stainless steel mesh is used as a filter in the authors' perfusion system; when these experiments were being carried out, an attempt was made to maintain heparinization above 60 gammas/ml, as determined by repeated protamine titrations. Presently, levels of 80 to 100 gammas/ml (approximately 4 to 5 mg/kg heparin) are maintained during cardiopulmonary bypass because of this finding, which is in accord with that of Senning et al., who found that precipitation of blood constituents and uncontrollable postoperative bleeding appeared more frequently with heparin levels of less than 3.5 mg/kg. The above-described microinfarction may be partially responsible for the hematuria occurring during prolonged bypass.

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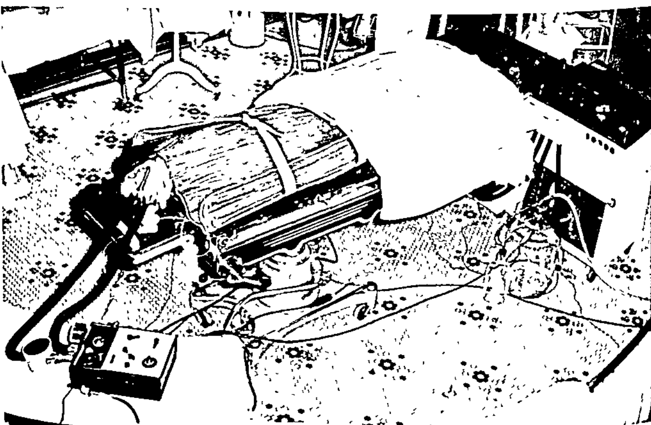


Fig. 6-86. The anesthetized and intubated patient is wrapped in the refrigerating blanket and a respirator is attached.

this blood for 24 hr Although the formed elements of the blood are better preserved with acid-citrate-dextrose (ACD), the acidity of the solution has raised questions concerning its use for this purpose. Studies of Zuhdi et al. (1960) indicated that citrated blood could be used for priming the perfusion system.

This laboratory has begun a study of this problem, so far, 10 dogs have undergone total body perfusion for 30 min at normothermic temperatures (Seidenstein et al) with blood collected in ACD solution B, as used in the Kings County Hospital Center blood bank, and stored for periods varying from 1 to 6 days. Four units of blood were used to prime the circuit. Thirty milligrams of heparin and from 0 2 to 1 0 Gm calcium chloride were added to each unit of blood Lead 2 of the standard ECG and femoral artery pressure were monitored throughout Serum potassium, sodium, carbon diox- ... plasma ... ined on ... t various the priming ... intervals before, during, and after perfusion, and on the donor dogs At the end of the perfusion, the excess heparin was neutralized with protamine. In addition, each dog received a complete blood coagulation workup before the perfusion and 2 hr after it.

Of the 10 dogs perfused to date, 9 survived; they were sacrificed at specific intervals. In 2 dogs there was evidence of a metabolic acidosis. In the others, metabolic alterations were minimal The changes in blood coagulation data obtained postoperatively in all the animals are similar to those seen when freshly drawn heparinized blood is used

From these results, it may be stated that it is possible to perfuse dogs with ACD blood and have them survive in good health It is appreciated that it is not possible to apply directly to human beings data obtained in these experiments in dogs, this problem is the subject of further study.

Glycerolized, frozen blood has been used by O'Brien and Watkins for perfusion Although these workers demonstrated that this blood was quite adequate for oxygen transport during bypass, the complexity of this method of preparation and a resulting shift to the left of the oxygen dissociation curve of the hemoglobin require further study

Edglugate-Mg was introduced for use in perfusion by Smith et al. partly to overcome the collection problems associated with the use of heparinized blood. Using this anticoagulant, it is possible to store blood up to 5 days and to use it for other patients if it is not needed for bypass. Studies in the authors' laboratory confirmed the usefulness of Edglugate-Mg and indicated that coagulation factors in animals a... perfusion were not unlike those following ... the ...

anticoagulant for bypass.

PARTIAL CARDIOPULMONARY BYPASS

Following extensive investigation in the experimental laboratory, the first clinical application of prolonged partial cardiopulmonary bypass was carried out at Kings County Hospital in 1954 (Newman et al.).

The patient was a 59-year-old housewife with known rheumatic heart disease of many years' standing, in whom a diagnosis of mitral stenosis and insufficiency, aortic stenosis and insufficiency, and tricuspid insufficiency had been made. Six months of intensive medical treatment at the hospital failed to free her of signs and symptoms of heart failure. Partial cardiopulmonary bypass was carried out at a rate which varied from 500 to 800 ml/min Clinical improvement lasted about 10 days, after which time her course went steadily downhill The patient died some 2 months following perfusion.

A second patient with intractable heart failure with a calcified, rigid mitral valve that had been operated upon at another hospital was similarly supported over a 3-hr period some months later, without the temporary improvement noted in the first patient

In 1956, the first of three patients with acute myocardial infarction and shock was placed on partial cardiopulmonary bypass for 3 hr (Stuckey et al , 1958). This patient recovered and is living, some 5 years later. A second patient lived for 9 days following perfusion, and a third, for 36 hr A fourth patient with the same preoperative diagnosis was perfused without improvement and had an extensive purulent pericarditis at autopsy. Three other patients were considered candidates for perfusion but died before it could be carried out (two of them died within 10 min after the perfusion team had been notified, and a third died within 30 min).

The selection of patients was made by the medical staff of Kings County Hospital with an effort to restrict use of partial cardiopulmonary bypass to patients with electrocardiographically demonstrated infarcts and a systolic blood

cated this same technique for correcting *valvular pulmonary stenosis* at normothermia, maintaining that a couple of minutes of inflow interruption is sufficient.

Swan et al. and the author (1956), independently, used hypothermia and inflow occlusion to perform open operations *on the aortic valve* as well, but the method is currently of historical interest only. Surgery on the aortic valve should be done with bypass techniques. A few other intracardiac lesions have been repaired with hypothermia and simple inflow occlusion, but currently, in the hands of most surgeons, hypothermia finds use only in combination with bypass techniques. Hypothermia alone at safe temperatures simply does not provide enough operating time. Still, hypothermia as a primary technique for open-heart surgery may receive further attention as more is learned about it.

Methods for supplementing hypothermia to permit a longer safe period of inflow occlusion have been advocated and should be mentioned. *Coronary perfusion* (Shumway and Lewis) as a supplement to surface cooling was logical because the heart, even more than the brain, seemed to be the weak organ. The heart was perfused with blood through the coronary circulation while the remainder of the circulation was stopped This helped There was a quicker return of a strong heart beat after a period of ischemia, and a slightly longer period of inflow occlusion was possible. Another technique to supplement surface cooling employed selective perfusion of the central nervous system, but this has not been used widely

A more intriguing supplementary technique that may possibly increase the usefulness of surface cooling is the use of *increased atmospheric pressures,* as recommended by Boerema. If an animal is cooled at 3 atmospheres of pressure, cardiac inflow may be interrupted safely for 45 min at a body temperature of only 27°C Apparently the tissues in these animals have become so saturated with oxygen in physical solution that they will withstand temporary ischemia very well. Also, enough oxygen may be carried dissolved in the plasma so that there is no need of hemoglobin at these high pressures. Technical difficulties associated with operating in high-pressure tanks may prevent practical application of this method, but it provides a direction for investigation and possible future development. For the present, hypothermia finds use in cardiac surgery principally as a supplement to extracorporeal circulation.

Open-heart Surgery with Pump-oxygenators and Hypothermia. All types of open intracardiac surgery have been done with a pump-oxygenator plus hypothermia. When pump-oxygenators first came into clinical use, many surgeons who had thought about this logical combination and discussed it actually tried to avoid the mild hypothermia that tended to develop, fearing that perhaps the dangerous features of both techniques would be compounded by linking them. Soon, however, clinicians (such as Sealy et al., 1958, 1959) followed the lead of Gollan (1959), a physiologist, who had long been using the combination of a pump-oxygenator and hypothermia experimentally.

With a heat exchanger in the return blood line or a device for cooling the entire oxygenator, the patient's core temperature could be rapidly lowered. Central temperatures below 30°C are achieved in a few minutes, and temperatures below 10°C can be reached, though 30 to 60 min of cooling may be required. Rewarming is carried out by pumping warm water through the jacket of the heat exchanger If blood temperature is kept above 0°C during cooling and below 45°C during rewarming, blood will not be damaged, though big, quick changes in temperature may cause bubbles to form (Donald and Fellows).

When body temperature is lowered during extracorporeal bypass, a decreased load is placed on the pump-oxygenator and lower blood-flow rates may be satisfactory. Furthermore, circulation may be stopped for relatively long periods to provide a completely dry and motionless field, if this is needed At temperatures below 15°C, for example, 30 to 45 min of circulatory interruption is possible.

At the present time, mild cooling with pump-oxygenators is used by many surgeons for a wide variety of intracardiac operations, and profound cooling, to temperatures of 20°C or lower, has been advocated for more complex repairs, such as those required for the tetralogy of Fallot (Gerbode et al, 1961). All the difficulties of this combined technique are not fully resolved yet, but it is a useful and promising method.

Open-heart Surgery with Autogenous Oxygenation and Hypothermia. Blood cooling may

trapped in the proximal aorta or major branches anc · there for at least 30 min.

of ...

oral artery with blood from the pump ... ator during cardiopulmonary bypass (Bagdonas et al., 1961b). The same body positions and the same system for monitoring air presenting in the common carotid arteries were used in this series as were used above. Under these conditions, it was found that the head-down position offers some protection against gas introduced into the femoral artery of the perfused animal. It was also noted that when air was introduced into the perfusion system through the femoral artery cannula, air emboli were consisten ... ed in the mesentery of the bowels b ... arteries, ... vations is apparent

HYPOTHERMIC PERFUSION. As described in Chap. 16, hypothermia combined with bypass has been the subject of considerable experimentation. Moderate hypothermia to approximately 32°C commonly occurs during perfusion if the apparatus is not heated. Recovery from this temperature is spontaneous, and no clinically significant chemical aberrations occur in the presence of good cardiac output after the perfusion.

Hypothermia of a profound degree combined with total bypass has been investigated extensively following initial studies by Gollan et al. (1952) and by Peirce and Polley, who demonstrated that the body temperature could be reduced to levels associated with cardiac arrest and could be rewarmed with survival. Cooling and rewarming were done with heat-exchanging apparatus through which the blood flowed during bypass, and circulation was maintained during cardiac standstill. Shields and Lewis cooled animals below 20°C in 10 min with a technique requiring cannulation of the right and left atria, pulmonary artery, and aorta, using the animal's own lungs for oxygenation. They turned off the pumps at this low temperature to arrest all circulation for periods up to 50 min, with survival. Gollan (1954) reported survival of a dog after 1 hr of cardiac arrest at 0°C. Clinical application of profound hypothermia with a pump-oxygenator was popularized by Sealy et al. (1958), who reduced the

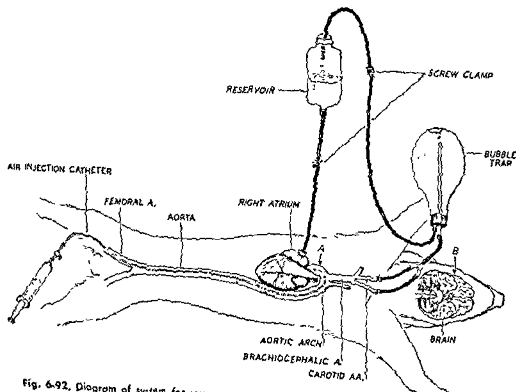


Fig. 6.92. Diagram of system for injection of air at the base of the aorta and for retrieving it from the common carotid arteries. A and B, points of reference for determining the levels

EFFECTS OF PERFUSION SYSTEMS ON BLOOD ELEMENTS

Recirculation of a known volume of blood through the apparatus at a known rate will allow assay of changes in red blood cells, white blood cells, platelets, and plasma proteins. The effects of pumps and oxygenators are separated by testing them singly and together.

A variety of pumps has been used in connection with various types of oxygenators with cardiopulmonary bypass systems. However, to the knowledge of the authors, no comparison of pumps under rigidly standardized conditions has been reported To obtain this information, three pumping systems (finger, roller, and diaphragm) were arranged in identical fashion except for the type of pump used in the system.

A single pool of blood was divided into three equal volumes to be pumped by each of the pumps against a pressure of 120 mm Hg, as determined by the height of the column of blood The pumping systems were operated simultaneously for 1-hr periods, samples were withdrawn at 1-, 15-, 30-, and 60-min intervals for determinations of plasma hemoglobin made by a method utilizing the Beckman spectrophotometer (Hunter et al). The method used for determining plasma hemoglobin should always be noted, otherwise these determinations are meaningless when an attempt is made to compare results obtained in different laboratories The results of low- and high-flow experiments are briefly tabulated below

TABLE 6-9. COMPARISON OF PUMPING SYSTEMS

Type	*Flow per min (avg), ml*	*Plasma hgb % (avg), mg*	*Index of hemolysis* *
Low Flow			
Finger (occlusive)	893	107	2.00
Roller (occlusive)	920	31	0 55
Diaphragm (valved)	860	61	1 14
High Flow			
Finger (occlusive)	2,081	121	1 02
Roller (occlusive) (priming vol., 1,250 ml)	2,166	48	0 37
Diaphragm (valved)	1,913	123	0 93

* Grams of free hemoglobin per 100 liters pumped.

The *roller pump* proved the least traumatic to red blood cells, as evidenced by the figures for plasma hemoglobin formed. As a result of this study, a roller pump has been incorporated into the authors' cardiopulmonary bypass system. A controlled test of pumping systems such as this is most useful for evaluating traumatic effects of whatever pump is used.

The pump-oxygenator now in use in the authors' laboratory is shown in Figs. 6-90 and 6-91.

Extracorporeal circulation results in *intravascular aggregation of erythrocytes* (*blood sludging*). Studies of Long et al. (1961) indicate that both in dogs and human beings, total-perfusion agglutination, as seen in the retinal and mesenteric arteries, is associated with an increase in high molecular weight plasma proteins and decrease in low molecular weight proteins. Addition of approximately 3 Gm/kg body weight of low molecular weight *dextran* (molecular weight, approximately 35,000) to the perfusate appears largely to prevent this agglutination and decreases the incidence of microinfarcts in the heart, liver, and kidneys Renal and hepatic function, as measured by usual methods, is not altered from that seen in perfusion without this material. The addition of this amount of dextran with low molecular weight resulted in lower plasma hemoglobin levels and less decrease in platelet count at the end of perfusion than occurred in controls. No unusual bleeding was observed with the use of this dextran. Hemodilution with other solutions (saline, albumin) also reduces intravascular aggregation, but the best prevention of this phenomenon has not yet been demonstrated.

The effects of oxygenators with an open blood-gas interface on plasma proteins has been studied by Lee et al. (1961) by circulating plasma through screen, disk, and bubble oxygenators Ultracentrifugation, viscosimetry, sulfhydryl group analysis, and histochemical analysis of the plasma indicate that insoluble denatured protein is produced, which is capable of producing sludging of blood. This denatured plasma may become serologically incompatible with previously compatible blood types, and contains conglomerates of chylomicrons, large enough to plug small blood vessels. The plasma was recirculated for 12 hr for these studies. The clinical significance of this finding is not clear, but it is inferred that membrane oxygenators may be more physiologic.

trapped in the proximal aorta or *major branches* and *may remain* there for at least 30 min.

A further study was concerned with the *fate* of controlled amounts of air entering the femoral artery with blood from the pump-oxygenator *during* cardiopulmonary bypass (Bagdonas et al, 1961b). The same body positions and the same system for monitoring air presenting in the common carotid arteries were *used in this series* as were used above. *Under these* conditions, it was found that the head-down position *offers some protection* against gas introduced into the femoral artery of the perfused animal. It was also noted *that* when air was introduced into the perfusion system through the *femoral artery cannula*, air emboli were consistently observed in the mesentery of the bowels *before* appearing in *the common* carotid arteries. The clinical implication of these observations is apparent.

HYPOTHERMIC PERFUSION. As described in Chap 16, *hypothermia combined* with bypass has been the subject of considerable experimentation Moderate hypothermia to approximately 32°C commonly occurs during perfusion if the apparatus is *not* heated Recovery from this temperature is spontaneous, and no clinically significant chemical *aberrations* occur in the presence of good cardiac output after the perfusion.

Hypotherma of a profound degree combined [illegible] the body *temperature could* be [illegible] and *rewarming* were done with [illegible]ing apparatus *through* which the blood flowed *during* bypass, and circulation was maintained during cardiac standstill. *Shields* and *Lewis* cooled *animals* below 20°C in 10 *min* with a technique requiring cannulation of the right and left atria, *pulmonary* artery, and aorta, using the animal's own lungs for oxygenation. They *turned off the pumps* at this low temperature to arrest all circulation for periods up to 50 min, with *survival. Gollan* (1954) reported survival of a dog after 1 hr of cardiac arrest at 0°C *Clinical* application of profound hypothermia with a pump-oxygenator was *popularized* by Sealy et al. (1958), who reduced the

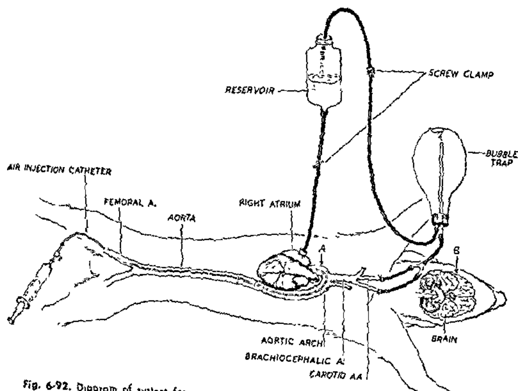


Fig. 6-92. Diagram of system for injection of air at the base of *the aorta* and for retrieving it from the common carotid arteries. A and B, points of reference for determining the levels.

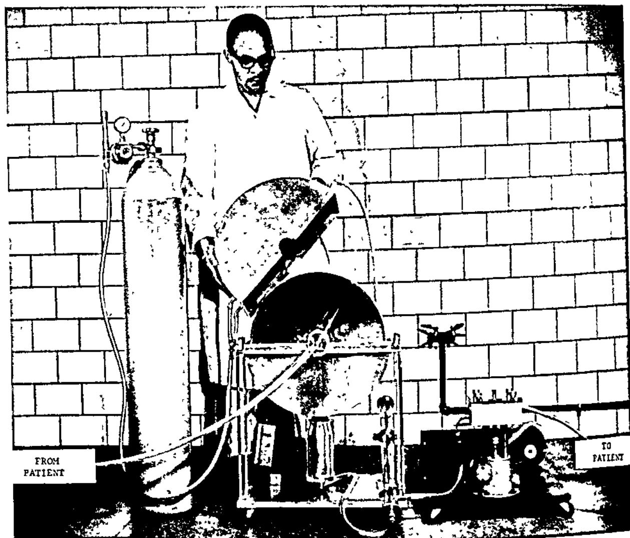


Fig. 6-91. Pump-oxygenator as in Fig. 6-90 except that the cover has been removed from the oxygenator to demonstrate the stainless steel disks.

HIGH-LEVEL HEPARINIZATION

The effects of heparinization at perfusion levels over a 4-hr period, without the complicating factor of perfusion, were also investigated in an effort to shed further light on the problem of hematuria during perfusions (Domingo et al.). Heparinization was maintained in dogs at 60 to 90 gammas/ml, as determined by repeated protamine titrations. Four hours of heparinization of dogs was found to be associated with progressively increasing *microscopic hematuria,* this was much less than the gross hematuria observed in patients placed on partial perfusion for the same period of time. No pathologic changes were noted in the lungs, kidneys, brain, heart, adrenal glands, or bladder. It appears, therefore, that heparinization alone does not result in changes in the kidney that could explain the hematuria. Observations on elements of the clotting mechanism during and following careful protamine neutralization.

four hours later, prothrombin activity is still no more than 70 per cent of the control level. Although the platelet counts are variable after heparinization, the average is reduced by at least 40 per cent. Other factors, such as clotting time, fibrinogen, fibrinolysis, and prothrombin consumption, are not significantly changed.

ANTICOAGULANTS FOR EXTRACORPOREAL CIRCULATION

Heparin has been used almost universally as an anticoagulant for the large amounts of blood necessary to fill the pump-oxygenator systems. There have been acceptably small alterations in acid-base balance associated with storage of

9 dogs died within the first 48 hr, 10 dogs lived 3 to 19 days, and 3 lived 20 to 30 days.

A purse-string suture in the mitral annulus was used to secure both types of prostheses in the mitral orifice following excision of the mitral leaflets. This method of fixation appeared to be one of the simplest, but the placing of this suture was not without problems. Care must be taken not to injure the circumflex artery, the aortic cusps, the coronary sinus, or the base of the aorta. One of these errors in technique was the most common cause of immediate death in these animals, it became less of a problem as experience was gained in placing the suture.



Fig. 6-94. Flop-valve type of prosthesis for mitral valve replacement.

One of the most important problems was thrombus formation in the left atrium and in the left ventricle adjacent to the base of the prosthesis, and the emboli which originated at these points. There were other problems related to the design of the valves and to the action of the valves on the formed elements of the blood. Currently a study is being made with valves fashioned from plastic materials. Such a valve without multiple components would appear to have many advantages.

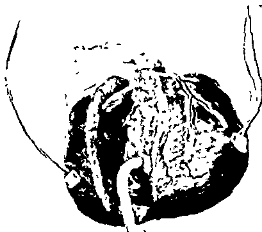


Fig. 6-95. Roving electrode positioned at a point on the right septal surface and reference electrodes sutured to the right and left ventricular epicardium.

A *ball valve* of similar design has been inserted into the mitral ring by Starr and Edwards. An attempt to eliminate thrombus formation at the site of fixation by incorporating flaps of plastic material to cover the suture appeared to offer some promise in preventing embolization from this site. Mitral valves constructed of *plastic cloth* of a design similar to that of the normal valve had been inserted by Kay et al. (1960), and of *flexible polyurethan* by Braunwald et al. (1960a). A high incidence of failure of insertion was experienced, and no dog survived more than 40 hr. However, a patient in whom this type of valve was placed was well 2 months postoperatively (Braunwald et al., 1960a). These valves require fixation of "chordae tendineae" made of fabric to the ventricular wall, as well as suture of the valve to the ring. Some success has been achieved in this direction, but the proper length of the "chordae" and their function when a large left ventricle changes in size have not been determined. Howard et al. replaced the mitral valve of dogs with a *homograft valve*, which functioned for 5 months in one animal.



Fig. 6-93. Ball-valve type of prosthesis for mitral valve replacement.

This experience indicated the feasibility of relatively long-term success if a proper valve is used. A prosthesis to replace a mitral valve should function satisfactorily for an indefinite period of time, be easily inserted, not cause thrombosis and resultant embolization, not cause stenosis or regurgitation, not injure or destroy elements of the blood, be well tolerated by the heart, function silently, be simple in

pressure below 80 mm Hg. These patients had failed to respond to intravenous 1-norepinephrine bitartrate (Levophed), had shown loss of consciousness and other signs of deterioration, and fell into a group in which the medical department of the hospital has established a survival rate of not over 15 per cent.

A total of six patients have been placed on partial cardiopulmonary bypass for periods of 3 to 7 hr, *all patients survived perfusion.* Among the problems posed by these perfusions are the effect of heparin on the size of the myocardial infarct, and the basic problem of whether or not partial cardiopulmonary bypass at the flows used in these perfusions reduces the work of the heart.

The Effect of Heparin on the Size of the Myocardial Infarct. One of the problems to be considered is whether or not the amount of circulating heparin required during perfusion would adversely affect the size of the infarcted area.

In a study carried out in the authors' laboratory, myocardial infarcts were produced in 38 dogs by ligating the anterior descending branch of the left coronary artery below the first major branch Heparin was given to three groups of dogs in a single injection of 5 mg/kg, (1) immediately postoperatively, (2) 24 hr postoperatively, or (3) 48 hr postoperatively These animals were sacrificed at various intervals, it was found that the size of the infarcts did not differ from those of the control animals which had received no heparin

From the above, it was concluded that the heparinization associated with partial cardiopulmonary bypass should not lead to an increase in the area of myocardial infarction.

Effect of Partial Cardiopulmonary Bypass on Cardiac Output. During the past several years, much has been written on the question of whether partial cardiopulmonary bypass alters cardiac output. At this time, there is no general agreement on this important point

The authors' laboratory has performed experiments with partial perfusion in the open-chest dog, controlling temperature, total body blood content (by placing the animal on a sensitive balance), venous pressure, and arterial pressure. Over 200 determinations of cardiac output have been made, shunting the total aortic blood flow through a Starling flowmeter attached to the aorta with isodiametric cuffs. In 13 pairs of determinations, identical weights have been observed within a few moments of shunting blood flow through the flowmeter with and without perfusion, all but one have shown a definite reduction in left ventricular external work per minute when assistance has been provided by the pump-oxygenator The combined pump and cardiac flow is usually less than the unassisted cardiac output, especially in the hypovolemic dog If body blood content is not controlled, cardiac output varies by a minute volume approximately equal to the variation in body blood content. This most important problem is under further investigation.

TOTAL CARDIOPULMONARY BYPASS

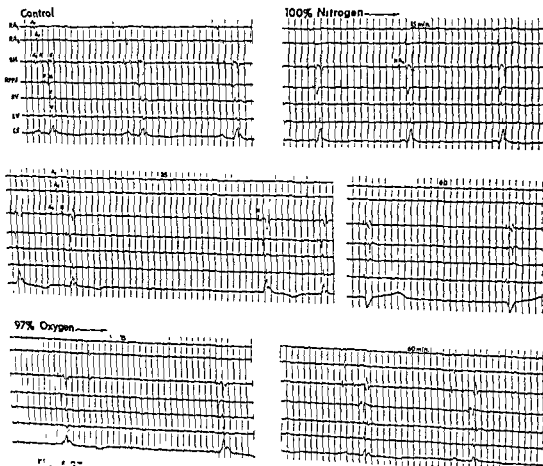
Studies of the Perfusion System. AIR EMBOLISM. Air embolism, whether introduced by the perfusion apparatus or at the operative site, continues to be a most important problem to those working with cardiopulmonary bypass. The authors' laboratory has reported the insidious and often lethal damage that may result from cerebral air emboli (Fries et al.). Air or oxygen introduced in a steady stream of small bubbles into the internal carotid artery of the dog results in a wide variety of clinical neurologic sequelae, which range from no apparent effect whatever to death in a few minutes A common chain of events is slow recovery from anesthesia, apparently normal postanesthetic behavior for a number of hours, then gradual loss of consciousness, and death. During this period, there may be abnormal neurologic signs. The EEG may be normal or abnormal. The only constant finding is brain damage in every animal at autopsy after death or sacrifice The goal is the complete elimination of this hazard, until this goal is achieved, it seems prudent to investigate certain aspects of this problem to determine what measures can be taken to reduce the hazards of air embolism

A study was made to evaluate quantitatively the effect of body positions ordinarily used in the operating room on the embolization of air from the base of the aorta (Bagdonas et al., 1960) Two milliliters of air was injected into the base of the aorta of dogs in which the level of the base of the aorta was varied in relation to the level of the head (Fig 6-92); the amount of air entering the common carotid arteries in each of five positions was determined by means of a bubble trap incorporated into the system It was concluded that the head-down position gives a relative protection from cerebral air embolism upon introduction of air at the base of the aorta, and that air can be

and of hypo- and hyperthermia (Stuckey et al., 1961c) on the specialized conducting tissue. It is desirable to obtain records from specific areas within the heart from unanesthetized animals with chronic heart disease; this has been done by bringing leads from the intracardiac electrodes through the chest wall to the body surface, where direct connections can be made to amplifiers and the recording apparatus (Stuckey et al., 1961b). Experiments have been conducted using small transistorized amplifiers and transmitters, which are implanted beneath the skin of the chest and connected to the electrodes within the heart. By means of this device, the need for external leads is obviated

Only two aspects of this work will be commented on here. The fact that the specialized conducting tissue can be demonstrated with a surface electrode (Fig 6-95) was first employed clinically to map the margins of a congenital cardiac defect at the operating table (Stuckey et al., 1959). This technique should contribute to a better understanding of conduction pathways in these defects and give positive aid in planning the surgical repair.

In a study of the effects of ischemia (Fig. 6-96) and hypoxia (Fig. 6-97) on the specialized conducting system, it was found that atrial and nodal conduction were the most sensitive to ischemia and hypoxia The specialized conducting system, except for the AV node, was relatively resistant to



severe hypoxia with recovery. Electrodes, ... of the right ventricle, RV. Components of the electrograms not identified ... 2 cm from SA node, in Fig. 6-96 are labeled as follows. A_3, right atrium 2 cm from SA node. After 35 min of hypoxia, no clearly recognizable atrial activity was present. From 45 min until the end of the hypoxic period the pacemaker site probably was located in the left bundle branch or in the Purkinje system. Ventricular fibrillation did not develop during 60 min of severe hypoxia.

mperature of patients to 8°C with total arrest the circulation for 10 min.

Use of hypothermia, with the accompanying duction of metabolic requirements of tissue, s allowed employment of so-called "low-w" perfusion with apparently minimal manistations of anoxemia. A beneficial product of wer perfusion rates is safe employment of naller oxygenators with lower priming volne. Zuhdi et al. (1961) described an apparas that is filled with 5 per cent dextrose in ater to the exclusion of priming blood or multaneous transfusion of the patient.

The effects of hypothermic perfusion, parcularly at temperatures under 20°C, are not ntirely understood. Among them are *intravasular agglutination of erythrocytes, disturbance f enzyme activity,* and *continuing slow metablism* with accumulation of fixed acids if the ow is reduced too much, even at temperatures n the range of 10°C

The possibility that gas may escape from cold lasma during rapid warming is suggested by the ncreased solubility of gas in plasma at low temeratures. The oxygen content of the blood may inrease 5 vol per cent during cooling. Experiments o determine the effect on the brain of perfusion with cold blood (8 to 10°C) for rapid body cooling, and of rapidly rewarming the cold blood during perfusion, have been conducted Bypass conducted in such fashion that the normothermic brain was perfused directly with blood at 10°C before his blood could circulate through other tissues resulted in focal destruction of the blood-brain barrier as evaluated with circulating fluorescein (Hodges et al) Cooling the animal to 10°C by partial bypass via the femoral artery, so that the cold blood did not reach the brain until the esophageal temperature had dropped to less than 20°C (when cardiac arrest occurred), resulted in no evidence of brain damage as evaluated by this technique. On the other hand, if cold oxygenated blood was warmed more than 10°C during one passage through the heat exchanger and allowed to perfuse the brain directly, evidence of focal brain damage was present Reducing the brain temperature to between 10 and 20°C did not yield evidence of brain damage as determined by this technique if the cold blood was not allowed to warm more than 10°C or was not allowed to perfuse the brain directly if this gradient was exceeded An adequate bubble trap between the heat exchanger and the arterial inflow prevented this brain damage on rewarming, even when this gradient was exceeded. In vitro studies demonstrated that gas bubbles form in the blood when it is warmed more than 10°C in one passage through the heat exchanger (Pollard et al).

STUDIES EMPLOYING TOTAL BYPASS

Transplantation of the Heart

Webb et al. have transplanted the heart, cooling the donor heart by perfusing it with cold Tyrode solution containing 10 per cent serum, both to refrigerate it and to remove blood from the vessels in order to prevent intravascular clotting during the absence of blood flow.

With the recipient on bypass, they anastomosed the venae cavae, pulmonary veins, aorta, and pulmonary artery, making some of these connections with mechanical couples. The longest survival after this procedure was 7½ hr.

Lower and Shumway have also employed hypothermia and bypass for cardiac transplantation. After bypass had been instituted, the heart of the recipient was excised, dividing the aorta and pulmonary artery, and leaving in situ the common posterior atrial wall with the venae cavae, pulmonary veins, and a ridge of atrial septum. The donor heart was excised from the hypothermic animal in a similar fashion, cooled further by immersion in 4°C saline solution to 12 to 15°C, and then sutured into place. Five of eight consecutive recipients survived 6 to 21 days, regaining normal activity and exhibiting remarkably normal ECG patterns. The pulse rate was variable and increased somewhat with exercise.

These hearts were rejected according to anticipated immunologic responses, although at variable time intervals. It might be anticipated that these problems of rejection will be overcome, in this light, these experiments have fascinating implications.

Mitral Valve Replacement. Over a period of several years, the authors' laboratory has had considerable experience with replacing the mitral valve in dogs with various types of prostheses

The first of these, a *ball-valve* type (Kernan et al), consisted of a casing made of Teflon and a Lucite ball (Fig. 6-93) In a series of 18 dogs in which this valve was used to replace the mitral valve, 5 died within 48 hr, 12 lived 2 to 21 days, and 1 died after 4 months

The second type of prosthesis was a simple *flap-valve* type (Berg et al) made of stainless steel (Fig 6-94). In a series of 22 dogs in which this valve was used to replace the mitral valve,

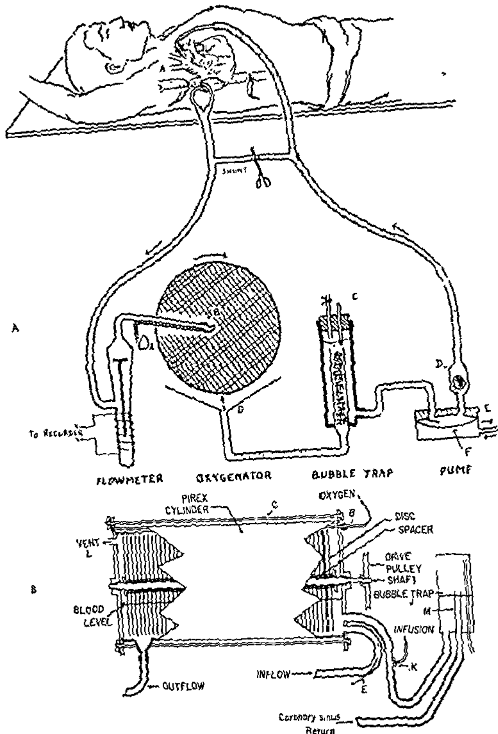


Fig. 6-99. A. Diagram of pump-oxygenator assembly for total body perfusion, as developed by Dennis and his associates. Blood is passed by catheters from the venae cavae to rotating screen B in an oxygen-containing case. After removal of gas in a collecting chamber C, the blood is pumped back to the arterial system. The pump F is emptied by compressed air. Regurgitation is prevented by a nylon shuttle valve D. (Courtesy of Levowitz et al. J Thoracic Surg. 1956) B. Diagram of the Kay-Cross version of the Björk oxygenator. Coronary sinus return passes through a reservoir and bubble trap before entering the oxygenator chamber with the caval blood. The disks mounted on a shaft are rotated at a selected speed by a motor. Blood leaving the other end of the oxygenating chamber is pumped back to the arterial system of the patient. (Courtesy of Cross et al. Proc. Soc. Exper. Biol. & Med. 1956.)

design, and be available at a reasonable cost. Progress has been made in this direction, but much remains to be done.

Studies of Cardiac Conduction. During the past 3 years, the Department of Surgery and Dr. B. Hoffman in the Dept. of Physiology (University of New York, Downstate Medical Center) have cooperated in a study of conduction within the heart with emphasis on the specialized conducting system. By utilizing total cardiopulmonary bypass, it is possible to open all chambers of the heart, position surface electrodes at specific points, and carry out studies precisely and unhurriedly (Stuckey et al., 1959). Electrograms may be obtained from the bundle of His (Stuckey et al., 1960), the right and left bundle branches, free-running Purkinje fibers, and the Purkinje-papillary muscle junctions, as well as other areas on the epicardial and endocardial surfaces of the heart.

By utilizing this technique, it has been possible to measure for the first time conduction time in the specialized conducting system of the in situ heart (Hoffman et al., 1959b), to study the activation of the interventricular septal myocardium during cardiopulmonary bypass (Amer et al.), and to study the effects of ischemia and hypoxia (Bagdonas et al, 1961a)

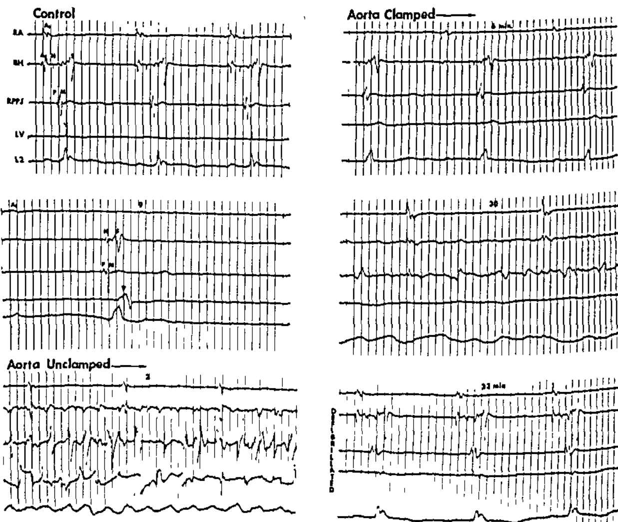


Fig. 6-96. Electrograms obtained at the indicated times during 30 min of ischemia and during a subsequent period of recovery. Electrodes are positioned as follows: right atrium near the SA node (*RA*), bundle of His (*BH*), right Purkinje–papillary junction (*RPPJ*), and epicardium of left ventricle (*LV*). L_2 designates lead II of a standard electrocardiogram. Components of the electrograms are labeled as follows: A_1, right atrium near SA node, A_2, right atrium beneath the His electrode; *H*, bundle of His; *S*, septum beneath the His electrode; *P*, activity in the Purkinje fibers; *M*, activity in the right anterior papillary muscle; and *V*, activity in the epicardium of the left ventricle. Ventricular fibrillation occurred at 13 min; note the persistence of Purkinje activity after 30 min of ischemia.

of oxygenator composed of a rotating spiral tube through which blood passed in an atmosphere of oxygen.

An ingenious type of oxygenator has been developed by Senning and Crafoord in Sweden, consisting of a series of transversely mounted, rotating, hollow cylinders with multiple perforations (Fig 6-100A) The blood is filmed as it passes across a tray in which a number of the rotating cylinders are mounted. A total perfusion, 4 hr in duration, employing the Crafoord-Senning apparatus, was reported by Andersen. Unfortunately, the patient did not survive.

BUBBLE DISPERSION. DeWall and Lillehei (1956) described their simple, disposable bubble oxygenator (Fig. 6-100B), which is based on principles evolved in t

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3,300 ml blood per minute and employing large bubbles and an antifoam compound was described by Cunbel and Englebet. The DeWall-Lillehei bubble oxygenator has received serious consideration by clinical surgeons everywhere because of

ing is derived from the patient himself after transfusion with acid-citrate-dextrose bank blood. Although excellent clinical results can be achieved with bubble oxygenators, as evidenced by the fine record of Lillehei and Cooley and their associates in more than 2,000 perfusions, most surgeons in the United States have come to use the rotating-disk oxygenator because of its dependability and excellent support of the patient in long perfusions. Experimental and clinical studies have revealed that excessive bubbling produces significant trauma to the blood. Enthusiasm for bubble oxygenators has been lessened also by the reports of embolization of antifoam A and gas to the brain.

MEMBRANE Theoretically the most physiologic of all oxygenators should be the diffusible membrane, and considerable work has been done in the effort to develop a practical membrane oxygenator.

... to Clowes for his excellent

membranes (Fig. 6-101A and B). Also deserving of recognition are Kolff et al. (1959) (Fig. 6-100C), Benvenuto and Lewis, Crescenzi et al., Dagher, Firme et al., and others. McCaughan et al. evaluated the various membranes suitable for oxygen diffusion, and Peirce has specifically evaluated Teflon membranes. Clowes and others have found greatest success with 0.5-ml Teflon sheeting. In reporting a membrane oxygenator developed by his associates, Gentsch discusses the problem of oxygenation by membranes, and notes the high cost of membranes, incidence of gas leaks through defects of the membrane, difficulty of sterilization, and limitations of output. In comparing the performance of a membrane and a disk oxygenator, consistently better values for pH, arterial, and venous oxygen saturation were obtained with the disk oxygenator

LUNG. Techniques have been described by Kantrowitz, Wesolowski et al. (1952a), Mustard et al., Bailey, Holt et al (1960), Read, Helmsworth et al. (1959b), and others, in which the lungs of the patient himself are employed to oxygenate the blood. These methods have limitations, mostly of a technical nature, and most surgeons have preferred to rely upon pump-oxygenators.

One must always recall the courageous pioneering work of Lillehei (1955) and his associates with methods of cross circulation, in which the lungs of the "partner" (usually a parent) oxygenated the

Fig. 6-100. A. Oxygenating unit developed by Senning. Blood moves forward from the rear portion of the covered tray and is oxygenated by a series of rotating cylinders. (Courtesy of Åke Senning, Extracorporeal Circulation Springfield, Ill., Charles C Thomas, 1958.) B. Diagram of helix-reservoir oxygenator developed by DeWall and his associates. The venous blood from the patient passes up the mixing tube, where it is in contact with bubbles of oxygen passed through a perforated disk of nylon or stainless steel. The blood then passes down a debubbling chamber coated with antifoam A, into the helix reservoir. This is usually maintained at 37°C in a water bath. The blood is then passed through a double filter back to the arterial system by means of the pump. The coronary suction unit is shown below. (Courtesy of De Wall et al. Surg, Gynec. & Obst. 1957.) (The helix-reservoir bubble-oxygenator components are made by the Phelan Manufacturing Co, Minneapolis, Minn, and Sigmamotor Inc, Middleport, N.Y.) C. Bubble oxygenator developed by Cooley and his associates The venous blood enters a mixing chamber of stainless steel into which oxygen bubbles enter through a perforated stainless steel plate. The blood spills into a debubbling chamber and thence into a spiral helix to the bottom of a reservoir, from which oxygenated blood is pumped back to the patient. D. Dismantled oxygenator of stainless steel. (Courtesy of Cooley et al. J. Thoracic Surg. 1958.)

ischemia; the peripheral Purkinje system was most resistant. Electrical activity was abolished in all portions of the conduction system with 40 min of ischemia. One hundred and twenty minutes of severe hypoxia abolished electrical activity in the atrium, while that of the specialized conducting system, exclusive of the AV node, was not markedly affected. *Ventricular fibrillation* consistently occurred with ischemia but not with hypoxia. The remarkable difference between the effects of ischemia and hypoxia would suggest that oxygen lack alone may not be so important in affecting the conduction system as other factors, such as the accumulation of metabolites and changes in pH and electrolytes.

CLINICAL STUDIES ON OPEN-HEART SURGERY AND CARDIAL BYPASS

It is difficult to realize that less than a decade has passed since the first successful perfusion of a human being with a pump-oxygenator for the open repair of an intracardiac lesion. It was in 1953 that, after many years of experimental development of a satisfactory apparatus for cardiopulmonary bypass, Gibbon repaired an interatrial septal defect in an 18-year-old girl In view of the obvious importance of the equipment, and in recognition of the many controversies that have been waged vigorously during the early years of clinical perfusion in favor of one type of pump or oxygenator over another, it would seem indeed appropriate to discuss the pros and cons of the various types of equipment.

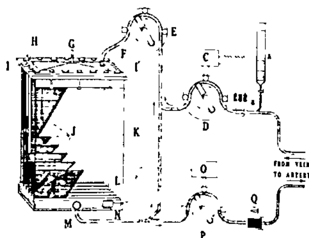


Fig. 6-98. Diagram of the extracorporeal system, developed by Gibbon and his associates Blood drawn from the venae cavae or blood reservoir *A* is drawn by a venous pump *D* to the oxygenating system. The recirculation pump *E* passes the blood to the top of the oxygenator, in which the multiple vertical screens *J* are set in an atmosphere of oxygen. The oxygenated blood may then be returned to the arterial system by another pump *P*. When the patient is not on cardiopulmonary bypass, the blood in the oxygenator system may be recirculated by pump *E*. (*Courtesy of Miller, Gibbon and Gibbon. Ann. Surg.* 1951.)

APPARATUS

Oxygenators. FILMING TYPES *Screen.* Many mechanical means may be employed to produce a sufficiently thin moving film of blood to permit efficient exchange of oxygen and carbon dioxide. Gibbon and coworkers (1951) developed an artificial lung that consisted of a series of vertically suspended stainless steel screens. A thin, evenly distributed film of blood flowed down these screens and was collected at the bottom in a fully oxygenated state for delivery by the pump back to the animal or patient (Fig. 6-98). Further refinements in the oxygenator were made by Kirklin and his collaborators (1958), from which evolved the Mayo-Gibbon apparatus Dennis and his colleagues combined the concepts of the screen and the disk. Venous blood was delivered near the center of large revolving disks of stainless steel screening The blood spread into a thin film as it ran slowly down the revolving screens (Fig. 6-99A).

Disk In 1948, Bjork presented a rotating-disk oxygenator. In this apparatus, small solid disks are mounted on an axle, which is rotated. The lower portion of the disk is immersed in blood, which moves slowly from the venous end of a chamber containing oxygen to the arterial end. A thin film of blood is picked up by the disk and oxygenated as it rotates through the bath. Variation in the capacity of the oxygenator can be achieved by changing the number of disks, the speed of rotation, and the volume of blood flow As with screen oxygenators, refinements developed subsequently, among the most significant being those of Cross and associates (Fig. 6-99B). By corrugating the stainless steel, Teflon-coated disks, it was possible to increase oxygenation by 40 per cent. The advantag
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ploying larger disks has been described by Osborn and associates The chief advantages of the disk type of oxygenator are its extreme reliability, ease of assembly, and lack of microscopic bubble formation.

Other Types Jongbloed developed a filming type

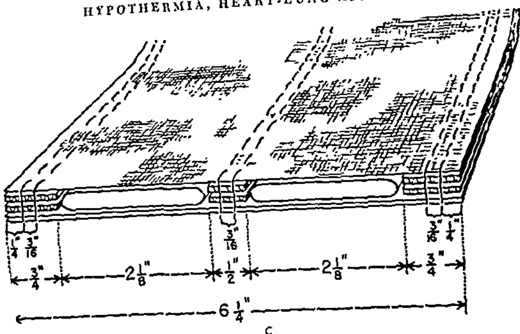


Fig 6-101. A Cross-section diagram of the multiple-unit membrane oxygenator showing the course of blood and oxygen flow. (*Courtesy of Clowes et al. J. Thoracic Surg. 1956.*) B. Diagram of a similar membrane oxygenator incorporated into a complete extracorporeal circuit, as developed by Glenn and his associates. (*Courtesy of Gentsch et al Surgery. 1960*) C. Cross section of membrane oxygenator developed by Kolff. There are three layers of fiberglass window screen, two tubes of polyethylene, and three pairs of spacers to allow space for the tubes to become distended with blood A 7-m length was rolled into a coil and then placed in a plastic bag containing oxygen. (*Courtesy of Effler et al. J. Thoracic Surg. 1956*)

priming volume further is commendable. The difficulty of cleaning and adequately sterilizing certain types of oxygenators has led to the development of disposable equipment

DISPOSABLE OXYGENATORS Perhaps the best-known and earliest disposable oxygenator was the bubble oxygenator of Tygon tubing described by DeWall, Lillehei, and their associates (1956) (Fig 6-100B) Through the use of appropriate reservoirs and filters it was possible to minimize danger from embolization of gas or antifoam A. Extensive studies of the physiologic effects of cardiopulmonary bypass with this apparatus were reported in 1956, by which time some 80 patients had been operated upon with this equipment Another disposable bubble oxygenator incorporated in a double plastic sheet was described by Gott et al. (Fig 6-102). This was subsequently employed very successfully by Cooley and by Sealy and his associates in infants with perfusions of short duration

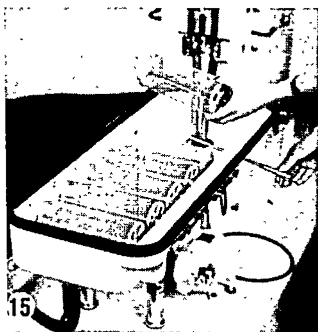
Disposable screen oxygenators have been described by Dutert The screens are composed of aluminum window screening set in a cast-vinyl box. The unit is of low cost and can be autoclaved. Osborn and associates (1959) described a disposable filming oxygenator constructed on a principle similar to that of the Gibbon oxygenator. Disposable vinyl plastic bags have been substituted for the screens. The clinical experience in 70 cases was encouraging.

A disposable, plastic rotating-disk oxygenator has been reported by Esmond and Cowley. Wilson and Vowles have described a unit functioning in a manner similar to that of the early Jongbloed type of oxygenator.

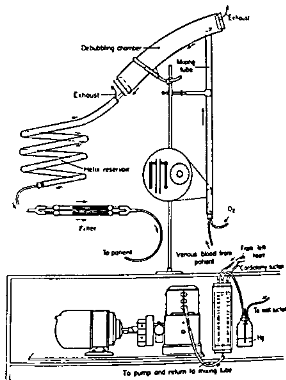
The membrane oxygenators are all disposable in that the membranes are used only once and then discarded. It has already been mentioned that the leak of oxygen through defects in the membrane and the high cost of Teflon film are objections yet to be overcome.

Pumps. A basic, simple discussion of the principles of pumps suitable for use in extracorporeal circulation was given by Bahnson and Melrose in 1958. Basic studies on various types of pumps revealed that adequate perfusion and maintenance of circulation could be achieved with either pulsatile or nonpulsatile pumps.

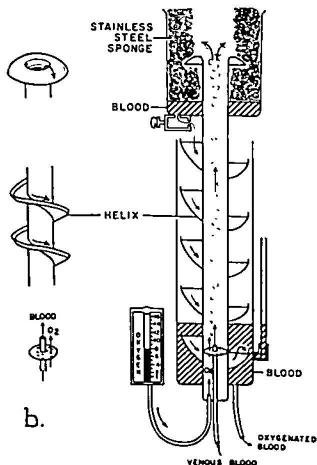
Essentially all the pumps employed for extracorporeal circulation should be categorized as pulsatile, but they differ in being of low amplitude or high amplitude. The former type of pump is


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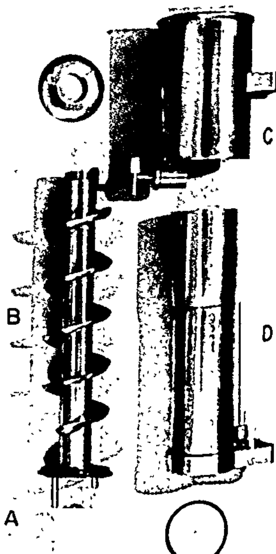
A


Exhaust
Debubbling chamber
Exhaust
Helix reservoir
To patient
Venous blood from patient
O_2
From left heart
Cardiotomy suction
To wall suction
Hg
To pump and return to mixing tube

B


STAINLESS STEEL SPONGE
BLOOD
HELIX
BLOOD
O_2
b.
OXYGEN
BLOOD
OXYGENATED BLOOD
VENOUS BLOOD

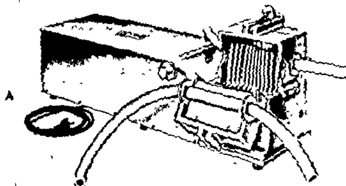
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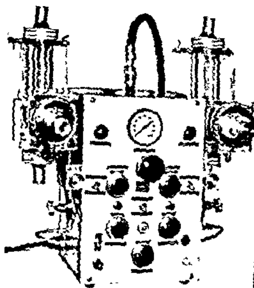

C
B
D
A

D

right atrium, through a septal defect to the left side of the heart, and thence to the *coronary* ar- [illegible] Fortunately, the patient recovered [illegible] severe central nervous system damage [illegible] postoperative period.

Inc[illegible] of large-caliber cann[illegible] from the [illegible] venous reservoir and thence to the oxygenator [illegible] 6-104C). *Adequacy* of venous return can be checked by momentarily occluding the *outflow* from the reservoir and noting how much blood enters the reservoir at a given time. *In addition,* the level *of* blood *in* the oxygenator must be kept *constant during* the perfusion to prevent either under- or overtransfusion. The importance of maintaining a stable venous pressure has been emphasized by Pence (1956b) and Kirby (1960) as a *means* of regulating the *blood volume* and the *rate of arterial perfusion.*





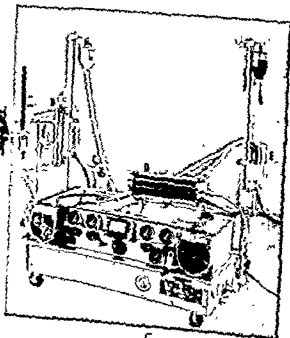
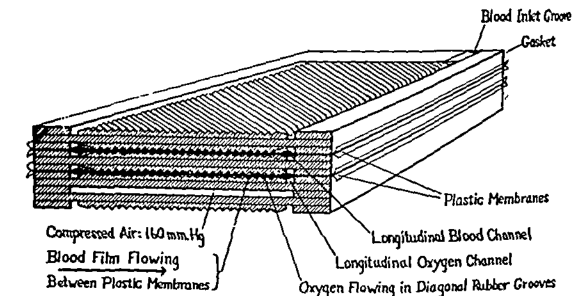


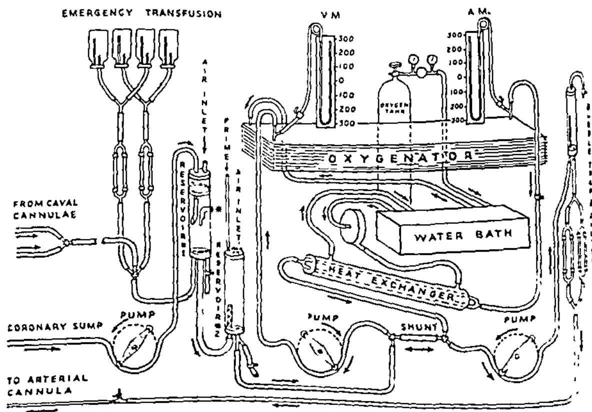
Fig. 6-103. A. Sigmamotor occlusive pump. Blood is propelled by pressure from oscillating metal fingers, shown in opened pump head. (Model T-M2, courtesy of Sigmamotor Inc., Middleport, N.Y.) B. Pump developed by Harken and his associates. Blood enters ventricles of plastic material with the direction of flow controlled by flutter valves. The filling and emptying speed and volume can be controlled by a piston that forces saline solution in or out of the chamber housing the "ventricles." (Courtesy of Davol Rubber Co., Providence, R.I.) C. Commercially available apparatus for extracorporeal circulation, showing DeBakey pump (A), heat exchanger (B), blood filter (C), Kay-Cross disk oxygenator (D), venous reservoir (E). (Courtesy of Pemco Inc., Cleveland, Ohio.)

blood of the patient Although more than 50 cases of open-heart surgery by this method were treated by Lillehei and his group, relatively few others employed it, because of its inherent disadvantages, the potential danger to the donor, and the rapid development of suitable pump-oxygenators. About this time, advances in the preparation of homologous lungs for oxygenating led to the brief clinical use of dog and monkey lungs as oxygenators.

In summary, one might say that many ingenious ways have been found to effect exchange of oxygen and carbon dioxide in the blood by mechanical equipment. Although not without problems, the disk-oxygenator nevertheless has emerged as the instrument most widely employed at present No one questions the fact that additional improvements are indicated in the design and function of oxygenators. Efforts must continue to be made to minimize trauma to the blood as reflected by the level of plasma hemoglobin, the presence of denatured proteins, the loss of platelets, and other modifications of the blood. The effort to reduce



A



B

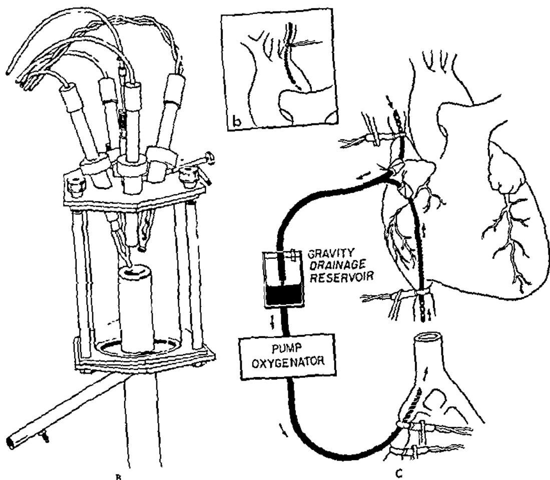


Fig. 6-104 A. Graphic representation of a patient on total bypass, showing the monitoring devices and arterial blood determinations. (Courtesy of Mendelsohn et al. *Surgery*. 1959) B. A monitor chamber developed by Clark and his associates The unit can hold four electrodes and a thermometer probe (Courtesy of Clark *Extracorporeal Circulation*, Springfield, Ill., Charles C Thomas, 1958) C A technique of total cardiopulmonary bypass for open-heart surgery The venous blood is drained by gravity siphonage. For most patients the arterial blood is returned through a femoral artery catheter. Occasionally the subclavian artery is cannulated for this return (Courtesy of Lillehei et al *J Thoracic Surg* 1958)

blood used to prime the oxygenator, and the trauma inherent in the pump-oxygenator equipment It has been possible to maintain the blood volume of most patients through blood-volume studies and the weighing of patients before and after operation, as well as by measurement of blood loss during the surgical procedure. Trauma to the blood by the pump-oxygenator has progressively decreased with refinements in the equipment, and it is customary to find less than 75 mg per 100 ml of free plasma hemoglobin after the period of total perfusion Red cell survival appears to be normal in patients for 2 weeks after perfusion and then shows an accelerated loss. The number of leukocytes usually drops moderately during perfusion and then returns to normal or slightly above Activation of the fibrinolysins has been reported by Osborn et al. (1955), as has abnormal consumption of prothrombin, by Perkins et al. Von Kaulla et al found a rise in prothrombin time in patients dying after cardiopulmonary bypass Battle and Hewlett summarized the changes observed as mild anemia, minimal hemolysis, leucocytosis, atypical lymphocytes, slight reticulocytosis, and minimal prolongation of the prothrombin time

Proteins. Denaturation of protein molecules

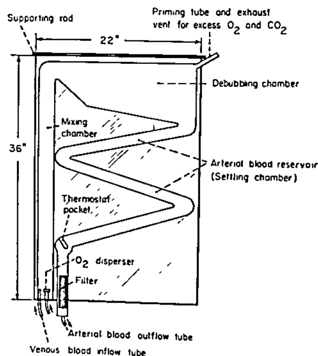


Fig. 6-102. Diagrammatic illustration of the plastic-sheet oxygenator (model IV) Blood passes up the mixing space, where it is mixed with bubbling oxygen before settling into the debubbling chamber, which is treated with antifoam A. The blood fills the settling chamber, passes through a filter, and is returned by pump to the arterial system (*Courtesy of Gott et al. Thorax. 1957.*)

exemplified by the rotating-roller type (DeBakey) (Fig. 6-98) and by the occlusive oscillating-finger type (Sigmamotor) (Fig 6-103A) Blood is propelled by an advancing pressure on the tubing supplied by either the metal roller or a bar Suitability of these pumps for use in cardiopulmonary bypass has been tested experimentally.

Ventricle pumps, representing modifications of the Dale-Schuster type, have been developed by Jongbloed; Dennis et al., Wesolowski et al. (1950, 1952b); Sirak et al. (1950), Dodrill et al (1952), and Hufnagel et al. (1958, 1959), Harken, and others have developed an excellent unit for clinical use (Fig. 6-103B). In this type of pump, a plastic or rubber chamber, often disposable, empties and fills, with or without electrocardiographic control, to deliver a stroke volume comparable to that of the beating heart. The artificial ventricle is emptied by external pressure from metal plates, gas, or liquid.

The low-amplitude pumps are at present the most commonly employed. Instead of the usual two-roller type, a single roller has been proposed by Esmond and colleagues (1961) As one reviews the literature, one can find essentially any combination of oxygenator and pump described, but currently the combination which is most commonly employed in clinical practice is the Kay-Cross rotating-disk oxygenator and the DeBakey pump (Fig. 6-103C).

Safety and Monitoring Devices. Interest in the incorporation of such devices in the pump-oxygenator has been evident since the earliest experimental work of Gibbon, Dennis, and others. Many of the earlier devices incorporated into the pump-oxygenators have been abandoned in an effort to make the equipment more simplified and foolproof. The manufacturer now generally incorporates specific devices as desired by the surgical team. Some of the modalities most often monitored have been described by Mendelsohn and associates (Fig 6-104A).

Several studies have supported the value of selective monitoring during cardiopulmonary bypass. Among the parameters most commonly measured are central venous pressure, arterial pressure, electroencephalogram, and esophageal or rectal temperature. There has been considerable development of equipment incorporated in the apparatus for the measurement of pH, pO_2, and pCO_2 and blood flow (Fig. 6-104B). Discussion of suitable devices and methods for the measurement or maintenance of blood flow through extracorporeal circuits is incorporated in the papers by Cordell and Spencer; McMillan; and Robicsek et al. (1961b), Albertal et al; Kirby (1958); and others.

Coronary Sinus Suction. All types of pump-oxygenator equipment include a system for the recovery of blood from the open beating heart. Since this is an obvious source of particulate matter and foam, and is a source of trauma to the blood because of the mixture of air and blood in the suction line, considerable attention has been given to the refinement of such a circuit. The principles to be embodied in an ideal system have been described by Winterscheid and colleagues. Special suction tips have been devised by Kirklin, Cross, and others in an effort to remove the intracardiac blood most efficiently.

Venous Drainage. Considerable discussion has centered on the best method of conducting blood from the venae cavae to the oxygenator. Most of the early equipment incorporated a pump for the withdrawal of venous blood under low pressure from the patient Such a method, however, causes more trauma to the blood by virtue of an additional pump which applies negative pressure. It increases the possibility of the entrance of air into the joints between the lines and the connectors if the ends of the cannulas in the venae cavae become obstructed There is also the danger that air may enter the lines through inadvertent reversal of the venous pump The author had one such experience, although the pump was promptly stopped, considerable air was pumped into the

ere a fall in platelet count and glucose level, id a rise in potassium and lactic acid concentrations (Fig. 6-105). A comparison of postoperative bleeding in 37 cases revealed no significant difference between fresh and stored lood The recommendations were that it was ife to use stored blood if it was not more than 6 hr old and if glucose was added after the rst 11 hr of storage

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paring 11 patients with heparinized blood drawn the afternoon before surgery and 8 patients with the modified ACD blood used to prime the oxygenator, it was noted that the postoperative drainage was twice as great in patients with the heparinized blood. Also, there was more plasma hemolysis and the platelet count was lower

In a previous report by Abbott and associates, a study was made of blood drawn with 25 mg heparin in 60 ml 5 per cent glucose in saline solution, either in plastic bags or silicone-coated bottles Blood collected more than 12 hr preoperatively proved to be satisfactory for clinical application

An Edglugate-Mg solution has been proposed by Brown and his colleagues to extend significantly the safe storage time for blood to be used in extracorporeal circulation In this formulation, sodium edathamil replaces sodium citrate, and magnesium chloride is added to inhibit inactivation of factor 5 by the edathamil Sodium gluconate and glucose prolong red cell survival After 3 to 5 days of storage of the blood, 15 mg heparin and 1 1 mM calcium ion as calcium chloride are added to each 500 ml. Clinical results with this solution have apparently been quite satisfactory

Because of the increasing number of patients with lesions that are amenable to surgical correction with the use of extracorporeal circulation, additional efforts have been made to modify the type and volume of blood used to prime the pump-oxygenator.

O'Brien and his coworkers (1960, 1961) have evaluated glycerolized frozen blood for extracorporeal circulation. The prolonged recirculation of thawed deglycerolized blood cells suspended in thawed heparin-plasma through a pump-oxygenator circuit resulted in no significant change of properties when compared with recirculated fresh heparinized blood. Their studies included evaluation of cell breakdown, gas transport, electrolyte concentrations, acid-base balance, and the deposition of fibrin upon the pump-oxygenator filter. Three patients underwent surgery for the repair of tetralogy of Fallot, aortic stenosis, and valvular pulmonic stenosis, respectively, with cardiopulmonary bypass in which this type of blood was used, and survived.

Mention has already been made of the pump-oxygenator developed by Panico and Neptune, which derives its priming volume from the patient himself after he, in turn, has been given 2 units of citrated bank blood intravenously.

MANAGEMENT OF THE PATIENT

Much has been said of the equipment and the physiologic alterations associated with extracorporeal circulation Probably of equal importance is a consideration of the personnel involved in operations requiring extracorporeal circulation. At first glance, it would appear that the demands on any hospital would be such as to limit the application of such methods to the major medical centers and university hospitals. However, Myerly et al have described their experience with extracorporeal circulation in medium-sized community hospitals.

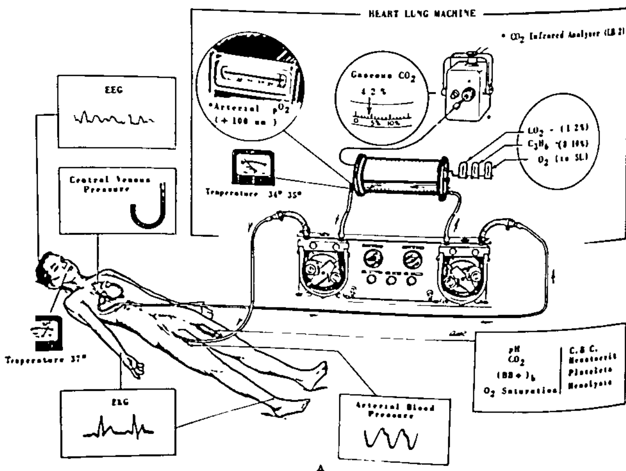
As in the larger hospitals, there should be a small, compact, and dedicated group of professional personnel. This clinical team should include a cardiovascular surgeon, cardiologist, internist, pediatrician, anesthesiologist, and radiologist, all well informed and interested in the field of extracorporeal circulation. Integrated into such a team should also be the senior nurse of the operating room and the person responsible for the maintenance and performance of the pump-oxygenator equipment, whether it be clinician or research fellow, nurse, or surgical technician. It is also advisable for the physician in charge of the cardiac studies of the patient to be a part of the team. This may be composed of an internist, pediatrician, or physiologist In hospitals with a program of extracorporeal circulation, it is most helpful to have periodic conferences attended by all or most of the team. However, final decisions relating to the specific therapy should be

PHYSIOLOGIC EFFECTS OF CARDIOPULMONARY BYPASS

Acid-base Balance. It had been demonstrated that an animal could survive on merely the venous return from the azygos system (Andreason and Watson). On this basis, Lillehei and his colleagues initially favored the use of low flows of 35 to 40 ml/kg, amounting to about two or three times the azygos flow. Clinical and experimental studies revealed a significant metabolic acidosis and increased morbidity and mortality rate associated with low flows. Kirklin and his associates (1958) did much to establish the value of employing a perfusion flow of 70 to 100 ml/kg, comparable to the cardiac output of the resting heart at normothermic temperatures. Under such conditions, no metabolic acidosis should result unless there is (1) low arterial saturation because of faulty function of the oxygenator, (2) excessive skeletal muscle activity during bypass, or (3) a prolonged perfusion. From extensive clinical studies by these workers and others, the acidosis was found definitely to be related to tissue hypoxia and to vary depending on the rate of perfusion and its duration. The major alterations observed were a postperfusion fall in plasma bicarbonate and a rise in lactic acid. Kolff and associates, during their early clinical experience, employed an infusion of sodium bicarbonate to combat the acidosis.

Electrolytes. Although the early studies of Varco et al. (1958) with low-flow perfusion indicated a decrease in level of serum potassium, significant abnormalities of serum electrolytes have not been observed with the use of high-flow perfusion.

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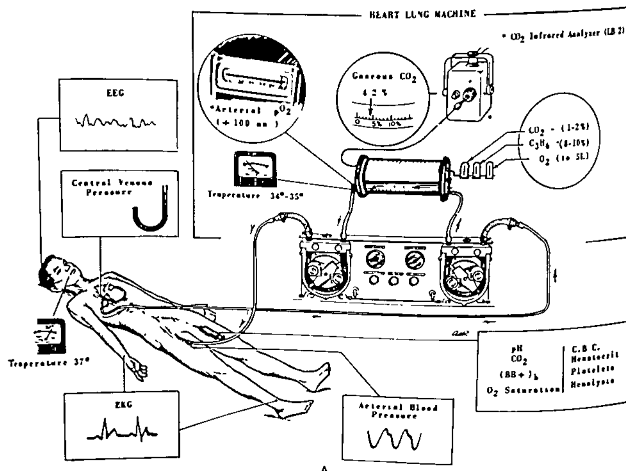
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the bilateral thoracotomy was generally employed, cannulation of the proximal stump of the left subclavian artery appeared to offer a suitable route for perfusion under pressure (Fig. 6-104C). In some patients, such cannulation was difficult and even dangerous because of apical pleural adhesions or a short artery with multiple major branching. In addition to possible ischemia involving the upper extremity, however, it was believed by many that cerebral complications were more likely, especially if a bubble oxygenator was employed. Indeed, many papers have been written on *cerebral embolization* of gas, fibrin, and antifoam A, experimentally and clinically. Consequently, there has been a tendency in the past few years to employ the common femoral artery (Fig. 6-104C). Even with this vessel, there have been serious complications from dislodgment of the cannula or dissection at the site of an arteriosclerotic plaque.

The technique of *caval cannulation* has remained reasonably standard, although initially there was some interest in the use of a single cannula which might be positioned so as to drain both superior and inferior venae cavae. In practice, it has been most satisfactory to introduce individual large-caliber catheters (plastic or metal) through the right atrial appendage or through openings elsewhere in the atrial wall (Fig. 6-104C). Caution should be taken not to advance the cannulas into the right jugular vein or hepatic veins. It is usually simple to localize the end of the cannula by palpation, leaving the tip with the side openings just beyond the level of the occlusive tapes about the venae cavae.

In patients in whom elective cardiac arrest is planned, it is generally wise to decompress the pulmonary bed, either by means of constant suction in the pulmonary artery or by a left atrial vent. The latter was well described by Kolff and Effler. A small catheter is introduced through the left atrial appendage into the left atrium and connected with the venous reservoir of the pump-oxygenator. The catheter is usually elevated about 15 cm above the heart level, so that blood drains out of the left atrium only when this pressure is exceeded. This had been employed for the same purpose previously by Sarnoff. Still earlier Gibbon et al. emphasized the desirability of venting the left ventricle, but primarily to prevent air embolization rather than to avoid overdistention.

Elective Cardioplegia. Shortly after successful clinical application of extracorporeal circulation, it was recognized that a still, empty heart would be necessary for the accurate repair of certain types of intracardiac lesions. Melrose (1955) described the use of *potassium citrate* solution to induce *cardiac arrest*



Fig. 6-106. A technique for inducing elective cardiac arrest. A noncrushing clamp is placed across the arch of the aorta. This suffices for anoxic arrest with or without topical hypothermic arrest. For chemical cardioplegia, the agent is injected into the aorta as shown. (*Courtesy of Effler et al. J. Thoracic Surg. 1957.*)

Early in their experience, both Lillehei et al. (1960) and Effler et al. (1957) employed potassium citrate as a 2.5 per cent solution in either blood or saline solution for cardioplegia (Fig. 6-106). Sealey, Brown, and their associates favored a mixture of potassium, magnesium, and neostigmine for arrest during the experimental and clinical application of extracorporeal circulation and hypoth[illegible] they have [illegible] ling car- [illegible] ly hypo- [illegible] followed [illegible] because of [illegible] complete and prompt cardioplegic action, the method has been generally abandoned because of increasing evidence of its deleterious effect on the myocardium.

One patient cited by Lillehei had cardiac arrest of 31½ min as a result of injecting 45 ml of a solution of 2.5 per cent potassium citrate for the correction of tetralogy of Fallot. Subsequently, the patient was admitted several times in congestive failure and died about 1 year later. The myocardium was pale and revealed diffuse widespread fibrosis as compared with a biopsy of the normal

at the interface between a gas and a liquid was observed by Bull and Neurath (1937). Lee and associates (1961) have described in detail the effect of pump-oxygenators in denaturing plasma protein. They considered this to be a significant factor in the morbidity and death associated with prolonged extracorporeal circulation. This may be one factor limiting the duration of successful cardiopulmonary bypass at the present time.

Electrocardiogram. Extracorporeal circulation per se has had insignificant effects on the electrocardiogram. Zimmerman and associates (1958) observed right bundle branch block in patients with surgery involving right ventriculotomy or resection of the pulmonary infundibulum. Such changes were not seen in closure of interatrial septal defect or in valvular pulmonic commissurotomy. Complete heart block resulting from damage to the bundle of His should be considered a surgical complication rather than a change associated with perfusion

Electroencephalogram. Extensive studies evaluating the effect of extracorporeal circulation on the electroencephalogram have been reported by Hodges and associates; Patrick et al.; and Kavan et al. The electroencephalogram appears to reflect the adequacy of the cerebral circulation, and in some patients, improvement over the preoperative tracing seemed to be a result of improved total circulation. Depression of the pattern can be noted readily with either an inadequate rate of perfusion or inadequate oxygen saturation. While major changes in the electroencephalogram are considered grave signs, the author has had two patients with "silent electroencephalograms" during operation, resulting from air embolization, who achieved very satisfactory neurologic recovery.

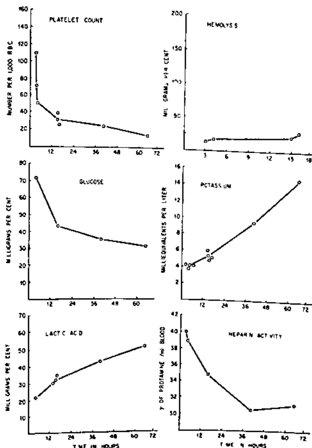


Fig. 6-105. A graphic summary of changes in stored heparinized blood. (*Courtesy of Lobpreis et al Ann. Surg.* 1960.)

Selective Blood Flow. Evaluation of the effect of artificial perfusion on blood flow through various organs has been studied, for the most part experimentally. Studies of blood flow through the liver have been reported by Waldhausen et al and by Andersen and associates, through the brain, kidney, intestine, and extremities by Halley and associates (1959), through the brain by Halley and associates (1958); and through the lung by Aletras and associates The circulation through the kidneys has been studied by Replogle and Gross, and through the kidneys and portal bed, by Jontz and associates Beall and associates studied the effect of total cardiac bypass on renal hemodynamics and water and electrolyte excretion in eight patients However, they employed the DeWall-Lillehei pump-oxygenator with a low perfusion flow of 35 ml/kg body weight per minute. No extensive clinical studies have been reported employing perfusion rates comparable to that of normal resting cardiac output of blood to individual organs

STORAGE OF BLOOD

Since in most oxygenators, the blood used for priming becomes an essential part of the circulating blood volume of the patient during cardiopulmonary bypass, the cellular and biochemical behavior of blood assumes prime importance An analysis of fresh and stored heparinized blood has been reported by Lobpreis and associates. The stored heparinized blood was drawn the afternoon prior to the day of operation into precooled, silicone-coated vacuum bottles containing 18 mg heparin and 30 ml normal saline solution. Storage was at 4°C, and analyses were performed on a total of 124 units of blood. The most significant changes

chips. No matter which method of cardiac arrest is employed, it would appear best to limit the period of arrest to less than 1 hr.

Congenital Defects. INTERATRIAL SEPTAL DEFECT. On the basis of embryologic development, the clinical cases of interatrial septal defect requiring closure have commonly been the *sinus venosus type* [Fig. 6-108(1 and 5)], the *secundum type* of the region of the foramen ovale [Fig 6-108(4)], the *primum type, supravalvular*, with or without a cleft of the leaflet [Fig. 6-108(3)], and the *endocardial cushion type* associated with partial or complete atrioventricular (AV) canal [Fig. 6-108(2)].

Ingenious and for the most part satisfactory blind techniques that were *most suitable* for correction of the *sinus venosus* and secundum types *of defect* are still occasionally employed by choice. These methods have employed an *atrial well, atrioseptopexy*, and *circumferential suture*. With the introduction of hypothermia, Lewis et al (1954), Swan et al. (1955), and others have successfully *repaired atrial septal* defects *under direct vision with temporary inflow occlusion*. For technical reasons or because of limitation in time, it *became* evident that safe and complete closure of the more serious and primitive defects (primum type and common AV canal) would have to depend on extracorporeal circulation

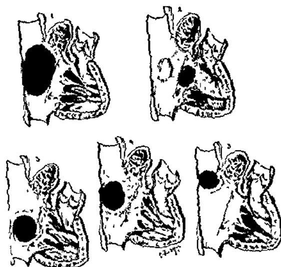


Fig. 6-108. Classification of types of atrial septal defects found *clinically*. 1. *Common atrium*. 2. Endo*cardial cushion* defect 3. Septum primum. 4. Septum secundum. 5. Sinus venosus. The dotted line identifies the atrial ventricular conduction system (Courtesy of *Watkins and Gross J. Thoracic Surg.* 1955)

Reports from clinics with large experience have indicated that the simpler defects can be closed *with little or no mortality and very brief perfusion* time, but in the more serious types there has been significant mortality. Cooley (1960) reported the closure of 110 secundum defects with no deaths but a 13 per cent mortality among 29 patients with an ostium *primum*. There is generally also a significant increase in mortality among patients who have developed moderate to severe pulmonary [illegible]

[illegible] Hg preoperatively. At 3 to 34 months following closure of the defect, the average fall in pressure was 72 per cent However, even in those patients whose pulmonary arterial *pressures were postoperatively* in the normal range at rest, there was a definite rise with exercise. In the experience of the *author, there* are certain patients with severe pulmonary hypertension *resulting from a patent ductus* arteriosus or an atrial septal defect in whom the hypertension is unchanged or becomes worse following correction of the lesion. Benjamin and associates suggested the use of an Ivalon patch with an 8-mm perforation to permit gradual adjustments of intracardiac and pulmonary pressures over a period of a few weeks as the hole in the patch slowly closed by thrombosis Bahnson and Williams *found minimal changes in intra-atrial* pressures following closure of defects in three patients with pulmonary hypertension, but a significant rise in the left atrial pressures in the remainder of 21 cases.

With the patient *on total cardiopulmonary bypass*, the right atrium is entered through a posterolateral vertical incision. It is possible to retract the caval catheters anteriorly to afford a complete view of the defect. Blood from the left atrium and coronary sinus *is gently aspirated and returned to* the oxygenator as described before. It is preferable to close the defects with two *rows of continuous* sutures rather than with interrupted sutures or the use of a plastic patch

With primum defects, *inspection should be made* for a cleft in the mitral or tricuspid leaflets (Fig. 6-109). If present, this should be repaired by interrupted sutures of fine silk. A patch may be em*ployed in these cases if suture* closure of the defect distorts the auricle or appears to *interfere with the* conduction bundle.

In a complete endocardial cushion defect (Fig. *6-110*), suture repair of the high interventricular septal defect *is first effected, followed* by repair of the clefts in both the mitral and the *tricuspid* septal leaflets. Following this, a patch is then most often used to close the atrial defect.

at the interface between a gas and a liquid was observed by Bull and Neurath (1937). Lee and associates (1961) have described in detail the effect of pump-oxygenators in denaturing plasma protein. They considered this to be a significant factor in the morbidity and death associated with prolonged extracorporeal circulation. This may be one factor limiting the duration of successful cardiopulmonary bypass at the present time.

Electrocardiogram. Extracorporeal circulation per se has had insignificant effects on the electrocardiogram. Zimmerman and associates (1958) observed right bundle branch block in patients with surgery involving right ventriculotomy or resection of the pulmonary infundibulum. Such changes were not seen in closure of interatrial septal defect or in valvular pulmonic commissurotomy. Complete heart block resulting from damage to the bundle of His should be considered a surgical complication rather than a change associated with perfusion

Electroencephalogram. Extensive studies evaluating the effect of extracorporeal circulation on the electroencephalogram have been reported by Hodges and associates, Patrick et al; and Kavan et al. The electroencephalogram appears to reflect the adequacy of the cerebral circulation, and in some patients, improvement over the preoperative tracing seemed to be a result of improved total circulation. Depression of the pattern can be noted readily with either an inadequate rate of perfusion or inadequate oxygen saturation. While major changes in the electroencephalogram are considered grave signs, the author has had two patients with "silent electroencephalograms" during operation, resulting from air embolization, who achieved very satisfactory neurologic recovery.

Selective Blood Flow. Evaluation of the effect of artificial perfusion on blood flow through various organs has been studied, for the most part experimentally. Studies of blood flow through the liver have been reported by Waldhausen et al. and by Andersen and associates; through the brain, kidney, intestine, and extremities by Halley and associates (1959); through the brain by Halley and associates (1958), and through the lung by Aletras and associates. The circulation through the kidneys has been studied by Replogle and Gross, and through the kidneys and portal bed, by Jentz and associates Beall and associates studied the effect of total cardiac bypass on renal hemodynamics and water and electrolyte excretion in eight patients. However, they employed the DeWall-Lillehei pump-oxygenator with a low perfusion flow of 35 ml/kg body weight per minute. No extensive clinical studies have been reported employing perfusion rates comparable to that of normal resting cardiac output of blood to individual organs.

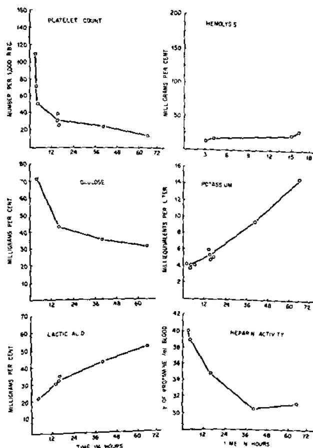


Fig. 6-105. A graphic summary of changes in stored heparinized blood. (Courtesy of Lobpreis et al Ann Surg. 1960.)

STORAGE OF BLOOD

Since in most oxygenators, the blood used for priming becomes an essential part of the circulating blood volume of the patient during cardiopulmonary bypass, the cellular and biochemical behavior of blood assumes prime importance An analysis of fresh and stored heparinized blood has been reported by Lobpreis and associates The stored heparinized blood was drawn the afternoon prior to the day of operation into precooled, silicone-coated vacuum bottles containing 18 mg heparin and 30 ml normal saline solution Storage was at 4°C, and analyses were performed on a total of 124 units of blood The most significant changes

chips. No matter which method of cardiac arrest is employed, it would appear best to limit the period of arrest to less than 1 hr

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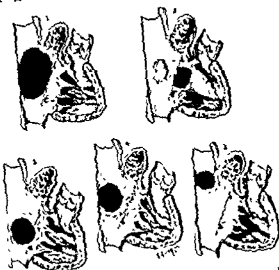


Fig. 6-108. *Classification of types of atrial septal defects found clinically. 1. Common atrium. 2. Endocardial cushion defect. 3. Septum primum. 4. Septum secundum. 5. Sinus venosus. The dotted line identifies the atrial ventricular conduction system. (Courtesy of Watkins and Gross. J. Thoracic Surg. 1955.)*

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delegated entirely to the responsible surgeon and the medical man. In a new and dramatic field, it is understandable that a number of surgeons in a given hospital may feel equally qualified to participate in such a program, but experience has generally demonstrated that the best programs are those controlled by one or two individuals The objectives and responsibilities of the internist in open-heart surgery have been described by Likoff and Winchell. With additions to and refinements in instruments and methods, it is increasingly possible to arrive at accurate anatomic diagnoses. Detailed consideration of the over-all management of patients undergoing extracorporeal circulation and intracardiac surgery has been made by Kirklin et al (1958), Lillehei et al. (1955), and Mendelsohn et al Before describing the specific existing surgical techniques for repair of intracardiac lesions with extracorporeal circulation, the specific maneuvers involved in supporting a patient with cardiopulmonary bypass will be discussed

SURGICAL MANAGEMENT

When a patient has been approved for open-heart surgery, certain technical preparations are necessary. Since patients with certain types of intracardiac lesions are predisposed to the development of *subacute bacterial endocarditis*, the question arises as to whether prophylactic use of antibiotic agents is to be recommended Kittle and Reed evaluated their clinical experience employing extracorporeal circulation with and without prophylactic antibiotic agents and found *the postoperative infection rate unchanged by the use of these agents* In the event of localization of infection in an intracardiac plastic patch with resultant septicemia, it has been found necessary in most cases to *reoperate* on the patient and remove the foreign material in order to control the infection Mortensen has called attention to bacterial contamination of oxygen used in perfusions, but this has not appeared to be a significant source of difficulty in clinical experience.

An estimation of the perfusion requirements is important, since an oxygenator of proper capacity, as well as cannulas of adequate caliber, must be selected beforehand Kirklin (1958) has discussed factors involved in providing the patient with an adequate perfusion As indicated before, most surgeons are now employing relatively high flows, approximating the cardiac output of the normal resting heart, when the operation is to be performed under normothermia. Flows of 60 to 75 ml/kg/min are desirable for adults, and 80 to 100 ml/kg/min for infants and small children. In other terms, a value of 2.2 liters/m² of body surface per minute for adults and up to 2.6 liters/m² of body surface per minute for infants has been recommended. The introduction of moderate to profound hypothermia associated with extracorporeal circulation has permitted significant reduction in flow and even cessation of the pump for periods up to 30 min It has been emphasized by Neville and his associates that *acidosis* may occur even with the body at 10°C.

The preoperative medication and preparation of the patient are similar to those of any patient on whom a major thoracic procedure is planned At the time of operation, an endotracheal tube is inserted, and the patient is maintained on *light general anesthesia* coupled with *relaxant drugs*, assuring adequate oxygenation Just prior to cardiopulmonary bypass, a transient state of respiratory *alkalosis* may be induced by hyperventilation since the lungs are left in a relaxed position throughout the period of cardiopulmonary bypass

The operative approach has changed somewhat during the past few years Surgeons initially favored a transverse bilateral anterior incision with transection of the sternum The incidence of pulmonary complications believed related to the difficulty of some patients in coughing or ventilating properly led to the suggestion by Julian (1957) and his associates that a midline sternotomy might be more suitable in most patients undergoing open-heart surgery. This approach was previously suggested by Schumacker (1953) for the Brock operation for pulmonic valvular stenosis and has received further

alone is to be entered Although morbidity appears to have been improved by the use of sternotomy, there is a greater problem from osteomyelitis of the sternum if infection develops. In some patients the sternal edges may slide on themselves before stability has been achieved, resulting in an unsightly ridge down the center of the chest

Special mention should be made of cannulation, since serious complications associated with arterial cannulation have been reported by Jones et al, by Thomas et al, and, with venous cannulation, by Bosher In the early years of perfusion, when

septum, where they may be multiple. Whereas in the earlier experience of most surgeons, these lesions were closed with patches of compressed [illegible] some type of fabric during a period [illegible]

[illegible] sible to avoid leaving a foreign body within the heart (Fig. 6-114B). Whenever feasible, cardiac arrest has been avoided as well.

One of the most serious complications associated with closure of the interventricular septal defect has been *complete heart block* resulting from injury to the bundle of His. The development and incidence of right *bundle branch block* have been reported by Bristow et al. and Dickens et al., and specific surgical maneuvers aimed at preventing damage t[illegible] has been described b[illegible] Robicsek [illegible] location of the [illegible] by Truex and by Reemtsma et al. Specific identification of the bundle by means of iodine staining has been reported by Allen, and by means of electrodes by Stuckey et al. (1960) and by Bonnes et al.

A significant contribution to the treatment of surgically induced heart block was rendered through the use of a *pacemaker* and myocardial electrode by Lillehei and his associates (Weirich et al., Thevenet et al.). With the heart rate electrically controlled, many patients regained a normal ventricular rate within several days, although a few patients required such support for a few weeks.

Although the mortality associated with repair of interventricular septal defects has been lowered to less than 15 per cent in patients over 2 years of age, the presence of significant pulmonary hypertension adds greatly to the risk. The transatrial approach for the repair of these defects in such patients has been associated with a definite lowering in mortality according to Starr, Kay et al. (1960), and Hudspeth et al. (Fig. 6-114C). Regardless of the specific surgical approach, a significant mortality may be expected when the pressures in the pulmonary artery and the right ventricle approach those in the systemic circuit, and a left-to-right shunt is minimal or absent.

PULMONIC VALVULAR STENOSIS. The transventricular valvulotomy of Brock and direct valvulotomy with hypothermia have represented distinct advances in cardiac surgery. However, the not-infrequent *association of pure pulmonic valvular stenosis with interatrial septal defect* has influenced many surgeons to repair the combined lesions with extracorporeal circulation. Generally the valve is approached through the pulmonary artery, and the commissures are cut open. Following this, the right atrium is opened and the septal defect closed.

More and more groups are employing extracorporeal circulation for the correction of pulmonary valvular stenosis alone. Gerbode (1960) has employed this technique in 29 of his 59 cases (Fig. 6-115A). There were no deaths among the last 16 patients in his series. Similar success has now been achieved by many others.

TETRALOGY OF FALLOT. Although the shunting procedures of Blalock and Potts continue to have a place in the surgical treatment of tetralogy of Fallot, the anatomic repair under direct vision is eminently preferable in most cases. The varying degree of severity of the anomaly-complex naturally influences the difficulty of repair and the risk of operation. The mortality in most centers has been higher with this type of case than with the other simpler anomalies, and is probably still higher when extracorporeal circulation is used than when the shunting operations are used. Lillehei and associates (1955a, b) reported their early experience in direct repair of anomalies of the Fallot type. As Kirklin (1959) indicates, it is often necessary to employ a patch in the high interventricular septal defect because of the overriding, and in certain cases it is necessary to employ an elliptical ventricular patch to enlarge the outflow path (Fig. 6-115B and C). As has been mentioned, considerable difficulty from blood loss through porous patches may be encountered. The special problems involved in patients who have had a previous Potts operation have also been discussed by Kirklin (1960). The adherence of pericardium to the myocardium makes exposure more difficult and adds the hazard of damage to the coronary vessels during dissection. In addition, the aortic pulmonary shunt adds to the difficulty of perfusing the aorta. Glotzer et al. (Fig. 6-115D) have described a direct and practical method of closing a patent ductus arteriosus via the pulmonary artery. This method may be applicable to the closure of the aortic-pulmonary shunt in patients undergoing open repair for tetralogy of Fallot.

In analyzing the factors affecting the survival

myocardium obtained at the time of operative correction. McFarland et al. studied the hearts of 19 patients in which potassium arrest had been induced for 6 to 67 min. In 15 there were microscopic areas of myocardial necrosis. The hearts of 11 patients in whom cardioplegia was not employed did not show these changes. Focal areas of necrosis in the hearts of dogs stopped with potassium citrate were also reported by Helmsworth et al. (1959a). In the measurement of transaminase in the blood of patients subjected to open-heart surgery with extracorporeal support, Quinn et al. found significantly elevated levels of serum glutamic oxaloacetic transaminase in the blood of patients subjected to potassium arrest in contrast with those patients who were operated on without arrest.

Acetylcholine has been favored by Lam et al. (1958), although they were originally equally interested in potassium citrate Studies by Greenberg et al. suggested that the effect on cardiac efficiency was as severe with acetylcholine as with potassium citrate (Fig. 6-107) Furthermore, it was usually impossible to obtain complete arrest with this agent as the heart usually responded by contracting sluggishly to mechanical stimulation *Anoxia of the myocardium* induced by cross clamping the thoracic aorta above the coronary ostia was found by Bhonslay et al to be an effective, rapid means of cardioplegia in experimental studies on cardiac arrest They employed anoxia with equal success in clinical cases with extracorporeal circulation, and subsequently many clinics came to prefer anoxia to potassium arrest. Studies of myocardial metabolism by Wallace, Willman, and Greenberg and their colleagues indicated that depression of the heart was less severe with anoxic arrest than with chemical agents

Induction of *ventricular fibrillation* during extracorporeal circulation was described by Senning (1952) and subsequently by Southworth and Peirce and by Glenn and Sewall Glenn et al. (1960) have continued to favor this technique, employing electric shock of 2 to 5 volts. Apparently the restoration of a normal rhythm by electric shock has not been a problem.

Hypothermic arrest was induced at low temperatures in rats by Niazi and Lewis and in dogs by Gollan (1954). In patients, through a combination of *anoxia and hypothermia*, cardioplegia has been achieved by various methods and appears to produce the least myocardial insult, according to comparative studies of myocardial metabolism. Hufnagel (1961) has reviewed the experience in inducing hypothermia by means of coronary perfusion with either cold blood or chilled Ringer's lactate solution. Success with this technique has been described by Heimbecker and Lajos. However, because of technical difficulties and local trauma associated at times with coronary cannulation, even with the development of special perfusion cannulas, there has been greater interest in the simple method of inducing cardioplegia through topical hypothermia by means of slush or ice

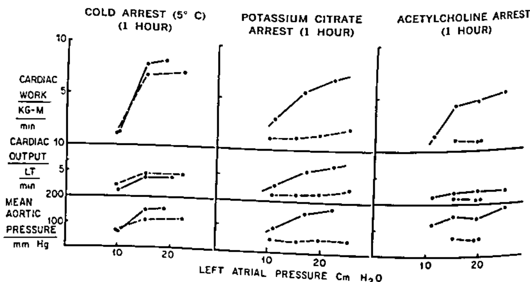


Fig. 6-107. Representative ventricular function curves, cardiac output, and aortic pressures in acetylcholine, potassium, and cold cardioplegia The solid lines represent prearrest control values (*Courtesy of Greenberg et al. Surgery*. 1960)

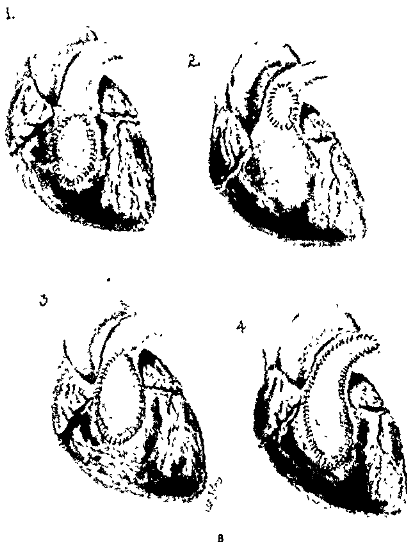


Fig 6-111. A. Clinical use of Ivalon patches (compressed from 12 to 1.5 mm) for closure of defects of the cardiac septa. (a) common atrium, (b) ostium primum interatrial defect, (c) defects of the membranous portion of the ventricular septum B. Clinical use of autogenous pericardium for enlarging the outflow tract of the right ventricle. (Courtesy of Sauvage et al. Ann. Surg. 1961.)

ANEURYSM OF THE SINUS OF VALSALVA Although an occasional case has been reported in which an aneurysm or fistula has resulted from a penetrating wound of the heart and aorta, most lesions involving the sinus of Valsalva have not been caused by direct trauma.

Weinberg et al. described aortic-cardiac fistulas resulting from open-heart correction of ventricular septal defect and tetralogy of Fallot.

Scott and his associates made a critical review of 43 congenital cases from the literature Of 34 aneurysms involving the right coronary sinus, 26 ruptured, 19 into the right ventricle and 3 into the right atrium Thirteen aneurysms involved the noncoronary cusp and all of these ruptured into the right atrium Only two involved the left coronary cusp and neither ruptured Repair has been relatively simple, involving excision of the aneurysm under direct vision, with extracorporeal circulation and suturing or patching of the aortic wall (Fig 6-119A and B).

Gerbode et al (1958) has reported five cases having a left ventricular to right atrial shunt. In these, the fistula between a defect of the septal leaflet of the tricuspid valve and a high interventricular septal defect was identified and obliterated during cardiopulmonary bypass.

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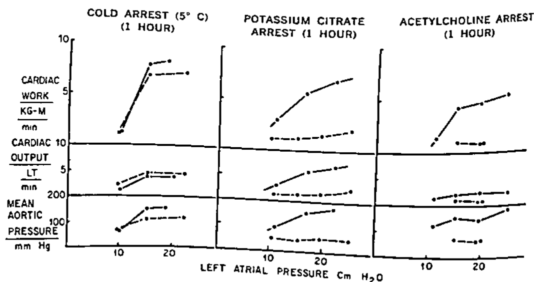


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Fig. 6-114. A Exposure of interventricular septal defect of the membranous portion by right ventriculotomy during temporary total cardiopulmonary bypass The cusps of the aortic valve may be seen through the defect B Closure of interventricular septal defect either by sutures alone or with a synthetic patch. (*Courtesy of Ethicon, Inc., Somerville, N.J. "Intracardiac Surgery with Extracorporeal Circulation."*) C. The right atrial approach to closure of high-pressure ventricular septal defects In some patients it is necessary to divide the septal leaflet of the tricuspid valve (*Courtesy of Kay et al, Surgery*, 1960)

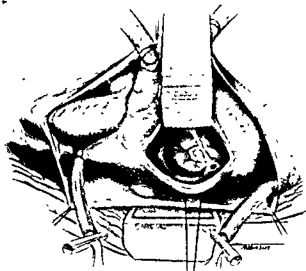


Fig. 6-109. The right atrium is visualized through an incision through its lateral wall A septum primum interatrial septal defect is shown, through which the mitral valve with a cleft in the septal leaflet can be seen. A narrow raphe separates this valve from the tricuspid valve. In many of these lesions, it is advisable to employ a patch for closure, rather than sutures alone (*Courtesy of Ethicon, Inc, Somerville, N.J. "Intracardiac Surgery with Extracorporeal Circulation"*)

There has been some discussion in the literature regarding the suitability of various materials for intracardiac patches The danger from synthetic patches in the presence of blood stream infection has already been mentioned Early trials of thin Ivalon for intracardiac patches occasionally ended in failure because of perforation of the patch On the other hand, Sauvage et al reported satisfactory experimental and clinical experience with the use of Ivalon compressed from 12 to 1 5 mm for intracardiac patches (Fig 6-111A) Autogenous pericardium for patches to enlarge the right ventricular outflow tract was also found to be satisfactory (Fig. 6-111B) Although Harkins et al considered pericardial patches satisfactory in the outflow tract of the right ventricle, one graft did show dilatation Edwards, Malm, Collins et al, and others have demonstrated satisfactory performance of Teflon fabric, which is currently in use in many clinics Cooley and associates have relied upon the knitted Dacron material used to fabricate their arterial grafts. There have, however, been instances of fatal hemorrhage through patches of porous fabric which were employed to enlarge the outflow tract Even after the cannulas were removed and the heparin neutralized with protamine sulfate or Polybrene,[1] the blood loss has on occasion continued with fatal outcome.

[1] Abbott Laboratories, North Chicago, Ill

Anomalous pulmonary venous drainage may be associated with interatrial septal defects When this involves the right superior pulmonary vein, as it often does, the orifice of this vein can be sutured to the rim of the ostium secundum, thus closing the septal defect and diverting the pulmonary venous blood into the left atrium by one maneuver

A much more serious situation is encountered with *total anomalous pulmonary venous drainage* The variations in this anomaly and methods of correction have been described by Cooley and Ochsner (Figs. 6-112 and 6-113).

INTERVENTRICULAR SEPTAL DEFECTS. The most effective means of correcting interventricular septal defects has consistently been with the use of extracorporeal circulation, with or without cardiac arrest. These defects are usually high in the membranous portion (Fig 6-114A) but may occur lower in the muscular

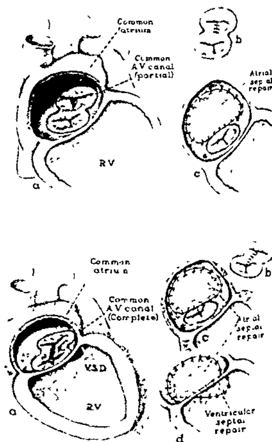


Fig. 6-110. Common atrium. *Above* a Lower portion of defect is similar to that seen in partial form of common AV canal b Suture of mitral cleft. c. New atrial septal patch in place. *Below* a. Lower portion of defect is similar to that seen in complete form of common AV canal b Suture of cleft in mitral and tricuspid valves. c. New atrial septal patch in place. d Closure of both atrial and ventricular septal defects (*Courtesy of Ellis et al. Surgery.* 1959.)

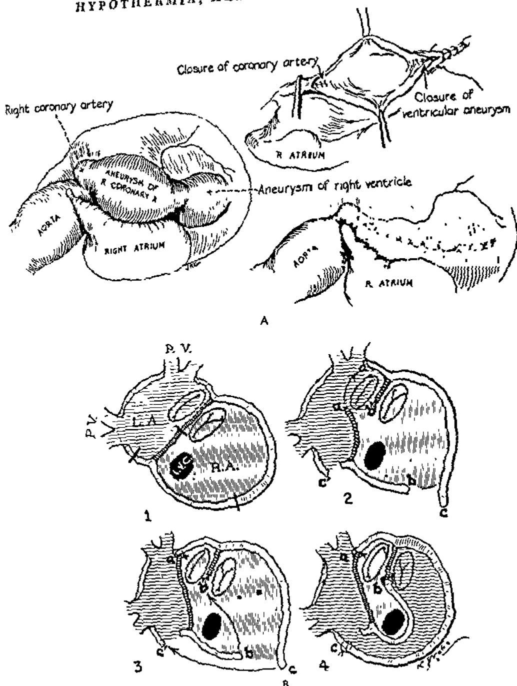


Fig 6-116. A. Aneurysm of the right coronary artery was opened with the aid of cardiopulmonary bypass. An opening 2 cm in length into the right ventricle was closed, as was the coronary artery near its origin. The edges of the aneurysmal sac were excised and oversewn. (Courtesy of Fell et al. AMA Arch Surg, 1958) B. Open intracardiac repair of transposition of great vessels employing the Senning operation by transplanting the anterior and posterior portions of the interatrial septum It is possible to create a new left atrium containing the pulmonary venous drainage and mitral valve. By approximating the lateral cut edges of incisions into the left and right atria (C' to C), a new U-shaped right atrium is created to contain caval drainage and tricuspid valve (Courtesy of Kirklin et al Surgery, 1961)

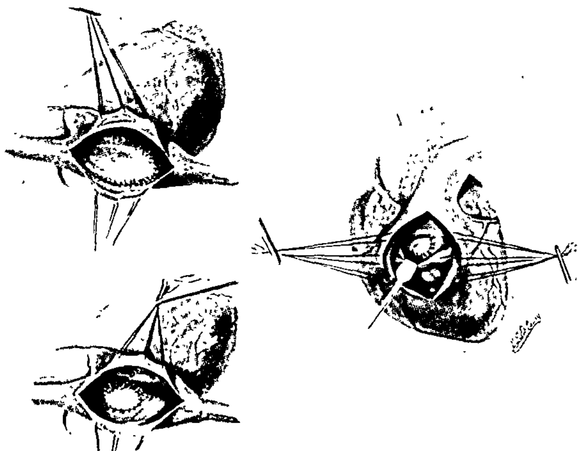
of patients with tetralogy of Fallot undergoing direct repair, Kirklin and his associates (1960) studied 110 patients. Operative mortality was specifically related to the degree of cyanosis. There was no mortality in 9 acyanotic patients, but 23 per cent mortality in 52 patients with severe cyanosis Age was another important factor, the mortality being 7 per cent in patients from 8 to 14 years of age and 100 per cent in patients under 2 years of age.

ARTERIOVENOUS FISTULAS AND ANEURYSMS OF THE CORONARY ARTERIES Fell and his associates reported on four patients treated successfully by surgery, two requiring extracorporeal circulation. In three cases, the right coronary artery was involved, in the remaining one, an anomalous branch of the left coronary artery was affected Definitive therapy consisted of excision of the aneurysm and division of the fistulous connections (Fig 6-116A).

TRANSPOSITION OF THE GREAT VESSELS. A number of ingenious techniques have been developed for the partial and complete correction of transposition of the great vessels Some of these, which attempt complete correction, have had clinical trial with limited success.

Kirklin (1961) has employed the Senning operation in 11 patients, with survival of 4 (Fig. 6-116B, A to F), utilizing extracorporeal circulation and profound hypothermia One of these patients later died of apparently unrelated causes. Up to the present time, palliative procedures that do not require cardiopulmonary bypass, such as the Blalock-Hanlon procedure (creation of an interatrial septal defect, Fig. 6-117), or the Baffes procedure (partial venous transposition, Fig. 6-118A and B), have seemed to be most helpful. Moss et al. reported success in three of six patients in whom, in addition to the creation of an interatrial septal defect, a branch of the right pulmonary artery was anastomosed to the azygos vein.

AORTICOPULMONARY SEPTAL DEFECT. Although certain of these cases can be handled adequately without extracorporeal circulation, the window type, occurring near the origin of the great vessels, is not well handled this way. Cooley et al. (1960) reported successful treatment of three patients, in two of whom he employed extracorporeal circulation and cardioplegia. These patients had an associated intracardiac septal defect.



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literature. These authors had success in surgical management with extracorporeal circulation. Kreel et al. had difficulty in correcting this type of lesion in a patient in whom a cusp was involved. The surgical results with subvalvular aortic stenosis have not been so encouraging and may call for the further development of procedures, such as insertion of an artificial valve between the apex of the left ventricle and the aorta.

Aortic Insufficiency. Aortic insufficiency has been difficult to manage surgically, and no significant degree of success has been achieved with blind methods. Although Garamella proposed removing an ellipse of the aorta and the noncoronary cusp to produce a competent bicuspid aortic valve, this technique has not been employed widely. It has been possible to suture a commissure with reinforcement by Ivalon or Teflon to produce a bicuspid valve. In some patients with an enlarged aortic ring, improved function has been achieved by annular plication or cusp suspension (Fig. 6-121A and B). With a scarred and contracted cusp, benefit has been reported through the attachment of a strip of synthetic material along the edge of the cusp (Fig. 6-122 A and B).

The development of ball valves and flexible cusps for partial or complete control of aortic regurgitation has culminated in successful clinical application. The most satisfactory valves have been those of Hufnagel et al. (1958b) and Harken et al. (1960). Methods of manufacture and problems associated with various prosthetic cusps or flap-valve replacements were described at the Conference on Prosthetic Valves (1961). Successful clinical use of certain of these methods has been reported (Fig. 6-122C).[2]

The operative mortality associated with aortic surgery in which prosthetic replacement is not employed has ranged between 15 and 30 per cent even in the best of hands.

Mitral Stenosis. The blind method of finger fracture or *commissurotomy* for mitral stenosis continues to be preferred by many groups for uncomplicated mitral stenosis. However, when mitral stenosis recurs, or when it is associated with a large clot in the left atrium, with calcification of the mitral valve, or with mitral insufficiency, open correction with extracorporeal circulation must be considered. Approach to the mitral valve from the right side, as first suggested by Bailey et al. (1952), has proved to be satisfactory in the author's experience, and orthodox cannulation can be easily performed (Fig. 6-123A). The aortic valve is readily accessible as well by the use of a median sternotomy. J. H. Kay et al. (1960), Effler et al. (1957), and others have favored approaching the mitral valve from the right side via the interatrial groove or septum. On the other hand, Nichols (1961) and Scott and others exposed the mitral valve from the left. The commissures are cut, taking care to leave the attachments of the chordae tendineae in their proper relationships along the edge of the cusp. In some instances, it is necessary to stretch the chordae, split the papillary muscles, or remove calcium from the cusps to produce a functioning valve.

Mitral Insufficiency. Many techniques have been developed for the blind correction of mitral insufficiency through the use of slings, baffles, circumannular ligatures, and annular plication. Under direct vision with extracorporeal circulation, insufficiency involving the posterior commissure is most easily improved by *annular plication* performed from within (Fig. 6-123B). In cases with contracture or destruction of a valve leaflet, *cusp extension* with some synthetic material, as described for the aortic valve, has been successful in some instances. In certain patients it has been possible to increase the area of the cusp by incising it in its midportion away from the attachments of the chordae tendineae and *inserting an elliptical patch.* Starr et al. (in press) have described a *shielded-ball-valve prosthesis* for replacement of the mitral valve, which has been used clinically. Experience in the open correction of mitral stenosis and insufficiency has been reported by many authors. The mortality is greater with correction of mitral insufficiency, and the best results range from 9 to 25 per cent or more. Because of unexpected findings often associated with mitral stenosis, Neptune has advocated that all mitral valve surgery should be performed with extracorporeal circulation.

As with the aortic valve, *partial or complete replacement* is seemingly the only choice in certain cases. The various experimental and clinical efforts in this direction were reported at the Prosthetic Valve Conference (1961).

[2] See also Part 7, Chap. 17 (Suppl. 1, 1962). *Editor*

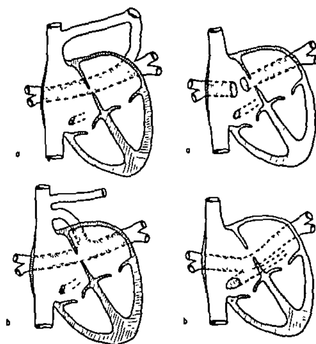


Fig 6-112. Drawings illustrating several types of total anomalous pulmonary venous drainage *Left.* a. The trunk enters the left brachiocephalic vein via a persistent left superior vena cava. b The trunk enters the posterior aspect of a normal right superior vena cava. *Right* a The pulmonary veins enter the right atrium directly b The veins empty into the coronary sinus, which drains at the usual site of the coronary ostium The author recently encountered a case which was a combination of left (a) and right (b). (*Courtesy of Cooley and Ochsner Surgery.* 1957)

Acquired Conditions. NONVALVULAR LESIONS *Aneurysm of the Heart* These lesions are generally a sequel to an extensive *myocardial infarction* involving the ventricular wall, although a rare case has followed a wound to the heart or insecure closure of a ventriculotomy. Schlichter et al. reviewed 102 patients coming to autopsy with aneurysm of the heart, 88 per cent died within 5 years of the onset of the condition, death being caused in a high percentage from congestive failure or systemic embolism A number of cases have been reported in which these aneurysms have been excised without extracorporeal circulation, but there has been the danger of embolism associated with the procedure or with incomplete excision of myocardial scar Cooley has described encouraging results in a series of patients in whom he achieved complete excision and firm repair with extracorporeal circulation and cardioplegia. He also encountered rupture of the ventricular septum following myocardial infarction resulting in an acquired interventricular septal defect. Correction of these lesions is essentially the same as that employed for the congenital type.

Myxoma. These benign tumors generally grow to a large size before they require medical attention by producing symptoms similar to those associated with mitral or tricuspid stenosis, or because of peripheral embolism A number of patients have been reported in whom removal was either attempted or successfully achieved without extracorporeal circulation. In many of the successful cases, hypothermia with inflow occlusion was employed. With tumors involving the left atrium, the safe and complete removal is most satisfactory under direct vision by left atrial approach with extracorporeal circulation. Cooley has reported success in 4 cases, and Tabor and Lam reported 11 cases, 6 of which were operated on with extracorporeal circulation. These tumors may be very friable and may be sessile, involving a large portion of the septum, or they may be pedunculated (Fig 6-120A). Kay and associates (1959) described

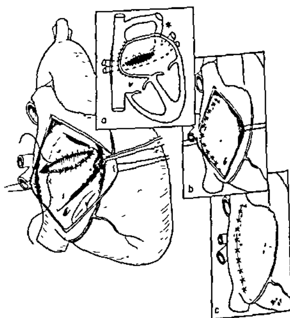


Fig 6-113. Method of repair of total anomaly of pulmonary veins using temporary cardiopulmonary bypass. An interatrial septal defect was enlarged to gain better access to the left atrium. A long incision was made into the common venous trunk to permit emptying of pulmonary venous blood into the left atrium. The atrial septum was then resutured so as to eliminate the defect and permit pulmonary venous drainage into the left atrium as shown. (*Courtesy of Cooley and Ochsner. Surgery.* 1957.)

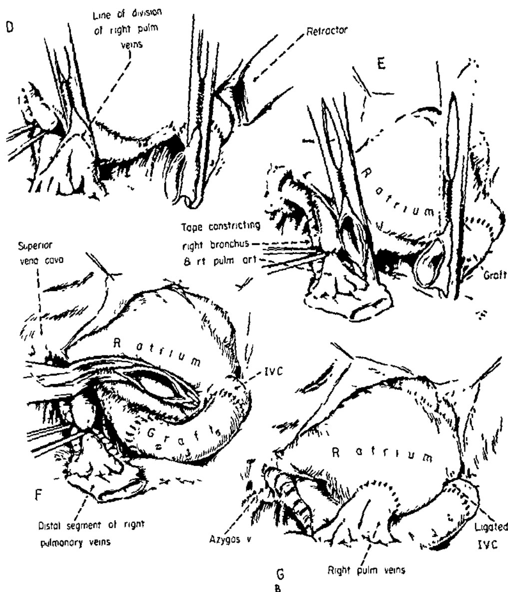


Fig 6-118. A. Transplantation of the inferior vena cava and right pulmonary veins in transposition of the great vessels By means of a graft, blood from the inferior vena cava is conducted to the left atrium through the stump of the right pulmonary veins *B* and C. B The distal segment of right pulmonary veins is then anastomosed to an incision in the posterolateral right atrium *D* and *E*. The inferior vena cava is then ligated between the insertion of the graft and the right atrium *F* and *G* (*Courtesy of Baffes et al J. Thoracic Surg.* 1957.)

proximating that of resting cardiac output. Under such circumstances, one would expect metabolic acidosis only if there is (1) low oxygen saturation from a faulty oxygenator, (2) excessive muscular activity of the patient, or (3) unusually prolonged perfusion

Cardiopulmonary Complications. In the initial group of perfusions there were a number of very serious and often fatal complications in the form of early postoperative *congestive pulmonary atelectasis* or *cardiac failure* Kirklin (1960) has discussed certain aspects of the *sudden-death syndrome* This sequence occurred rapidly, usually within 6 to 12 hr following perfusion, and was manifested by sudden restlessness, apprehension, and sudden death This appeared to be related to a drop-off in cardiac output In analyzing the course

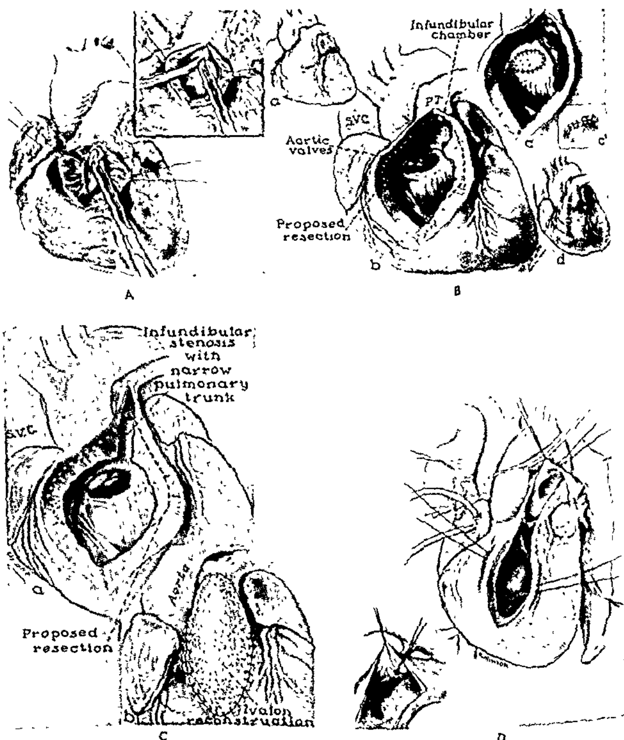


Fig. 6-115. A. Transventricular incision *showing* the inversion of the stenotic pulmonary valve into the *operative* field. *Insert:* The excessive infundibular muscle has been excised, and the valve is being opened laterally on two sides. (Courtesy of *Gerbode et al. Surgery.* 1960.) The author has preferred to open the pulmonic valve *from the* pulmonary artery unless ventriculotomy is necessary for other reasons. B. *Open intracardiac* repair of tetralogy of Fallot with infundibular chamber and wide pulmonary valve *ring and* artery (*a*) The unopened heart. (*b*) Pulmonary valvulotomy is performed where indicated The *ventricular* septal defect is prepared by direct suture *c'* or with compressed Ivalon sponge (*d*) Ventriculotomy is closed after excision of the hypertrophied *crista supraventricularis* C. *Open intracardiac* repair of tetralogy of Fallot without an infundibular chamber and with an infundibular *narrowing* going to the valve ring. Curved compressed Ivalon sponge is used to effect a *plastic reconstruction* and enlargement of the outflow tract. The incision is extended up into a narrow *main pulmonary* artery *b.* (Courtesy of *Kirklin et al. J. Thoracic Surg. 1959.*) D. Occlusion of the pulmonic *orifice* of the ductus is maintained with the index finger, while a purse-string suture is *placed* about the pulmonic orifice. (Courtesy of Glotzer and *Bloombert. J. Thoracic & Cardiovascular Surg. 1960.*)

of 34 patients, Boyd observed a poor outcome in those patients with cardiac output of less than 2 liters/min It was believed by some investigators that overoxygenation, occurring more readily with the bubble oxygenator than with the screen or disk type, was an important factor in such complications by virtue of oxygen toxicity or microbubbles. Since an oxygen tension of 500 mm Hg was believed capable of producing serious complications, the maintenance of oxygen tensions between 100 and 200 mm Hg was recommended. Subsequently, further consideration of oxygen toxicity by Maloney et al, Mendelsohn et al, and others has thrown considerable doubt on the role of oxygen toxicity. As mentioned before, it was noted by Effler (1959), Kolff (1958a, b) and their associates, and by others that prevention of left atrial or ventricular distention or the development of back pressure into the lungs from the left side of the heart was important in achieving good cardiac output after perfusion, and in the prevention of congestive atelectasis, particularly if cardioplegia was employed. Since employment of a left auricular vent, the author has noted a significant reduction in pulmonary complications, particularly in patients with pulmonary hypertension or induced cardiac arrest. In certain patients with advanced, fixed pulmonary hypertension, this state may continue or worsen following even the most excellent anatomic intracardiac repair

Complications related directly to surgical technique are *heart block* resulting from damage to the conduction system of the heart, *aortic insufficiency*, associated with injury to an aortic cusp, and *recurrent or residual defect*. Mortality from induced heart block has been greatly reduced through the use of myocardial electrodes and a *pacemaker*

Significant damage to aortic cusps during the repair of a high interventricular septal defect has often led to a fatal outcome from aortic insufficiency.

The author had an adult patient who developed a shocklike state early on the fifth morning following repair of a large high interventricular septal defect The shock responded to vigorous treatment by use of a pacemaker (a myocardial electrode was left in place at the time of surgery) and pressor agents. The patient subsequently revealed an aortic diastolic murmur and wide pulse pressure. It was presumed that a suture, passed through the base of the cusp, had created a late small perforation in one of the aortic cusps. The patient returned to a gainful occupation and was well 3 years later although he still had evidence of aortic insufficiency. Hanlon has described a case in which successful repair with a patch was achieved through reoperation.

Evidence of *residual shunt* was not uncommon in the earlier days of cardiac surgery, when great effort was made to operate with short perfusion time and to place sutures superficially, so as to minimize the danger to the conduction bundle. In some instances, there was disruption of the repair of the septum with the use of either sutures or a patch. Reoperation is indicated in such a situation, provided the condition of the patient is adequate. Callaghan and associates have described such an experience.

Embolism. Much was written in the early days of perfusion regarding *cerebral embolization* by antifoam A, fibrin, or gas. The cerebral complications associated with extracorporeal circulation have been described by Ehrenhaft. Venting or aspirating the left ventricle to prevent air embolization was described by Gibbon et al. (1939). The employment of the femoral artery, instead of the subclavian artery, for cannulation was another move aimed at reducing cerebral complications. The dangers from antifoam-A embolism were studied extensively, experimentally and clinically. In pump-oxygenators that require the use of this antifoam, the dangers have been significantly reduced through its proper application and the use of filters

Gas embolism to the brain or coronary arteries has been of special concern Management of air embolization to the coronary arteries was discussed by Lam et al. (1954).

Fig 6-119. A Technique of repair of a ruptured aneurysm of the sinus of Valsalva associated with an interventricular septal defect. Compressed Ivalon sponge was employed to close both defects after excision of the thin-walled aneurysm during cardiopulmonary bypass (Courtesy of McGoon *et al. Ann. Surg.* 1958.) B. Repair of an aortic right ventricular fistula via the right atrium. The aortic wall was sutured to the aortic valve ring with reinforcement by Ivalon sponge. (Courtesy of Spencer *et al* Ann. Surg. 1960)

a myxoma in the left ventricle, removed during cardiopulmonary bypass.

Aneurysms of the Thoracic Aorta. Resection of aneurysms of the thoracic arch employing extracorporeal circulation and perfusion of the carotid and coronary arteries has been attempted a number of times without success.

Although aneurysms involving the descending thoracic aorta can be satisfactorily excised and a graft inserted with a left atrium–to–femoral artery shunt, Gerbode et al (1957) have reported on the use of extracorporeal circulation in patients with traumatic aneurysms involving the descending thoracic aorta.

VALVULAR LESIONS. *Aortic Stenosis.* It is well known that many excellent results have been obtained with the blind commissurotomy or fracture performed via the left ventricle or ascending aorta However, failure to correct associated aortic insufficiency, the occasional production of significant aortic insufficiency, and failure to resuscitate a heart in which ventricular fibrillation has developed have been reasons for many surgeons to favor the use of extracorporeal circulation. Under direct vision, it is possible to apply the specific procedure most suited to the distorted and diseased valve. Such maneuvers include removal of calcium from the cusps, cutting the commissures under direct vision to their point of suspension, extension of leaflets, and cusp replacement (Fig. 6-120B). The risk involved in the treatment of acquired rheumatic and arteriosclerotic aortic stenosis is significantly greater than that connected with congenital aortic stenosis. Variations in the valve deformity associated with congenital aortic stenosis have been described by Spencer et al (1960).

McGoon et al. (1961) have described two types of supravalvular aortic stenosis, and Starr et al. (1961) added another variant as a result of reviewing 17 autopsied cases reported in the

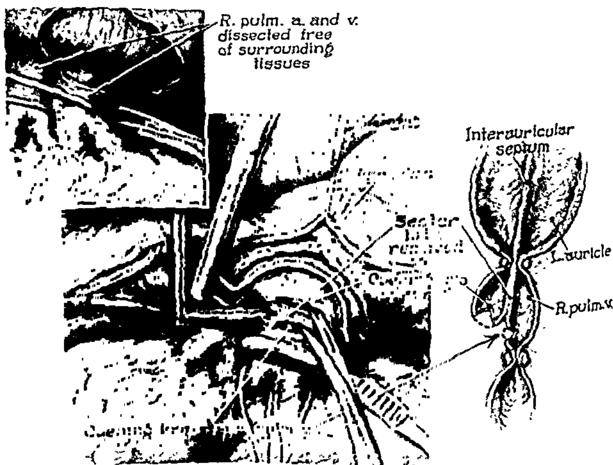


Fig. 6-117. Technique of creating an interauricular defect A special clamp is applied to compress the right auricle and superior pulmonary veins as shown By an incision in the right auricle and superior pulmonary veins the lateral edge of the auricular septum is exposed, from which a sector is removed to create the defect. (Courtesy of Blalock and Hanlon, Surg Gynec & Obst. 1950)

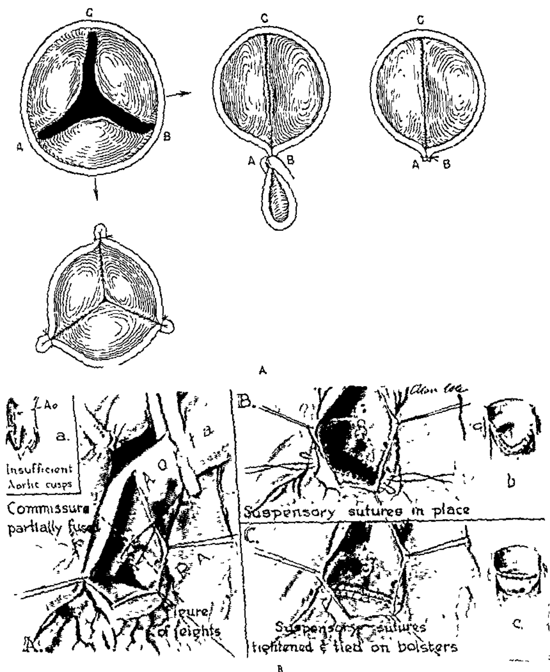


Fig. 6-121. A. Aortic insufficiency may be corrected by removal of the noncoronary sinus or by narrowing of the annulus by plication with mattress sutures at the commissures, as shown below. (Courtesy of Hufnagel Ann Surg 1959.) B. Aortic insufficiency may be corrected by completely closing a partially fused commissure A and by suspending the resulting two cusps B and C. (Courtesy of Anderson et al, Ann Surg, 1961.)

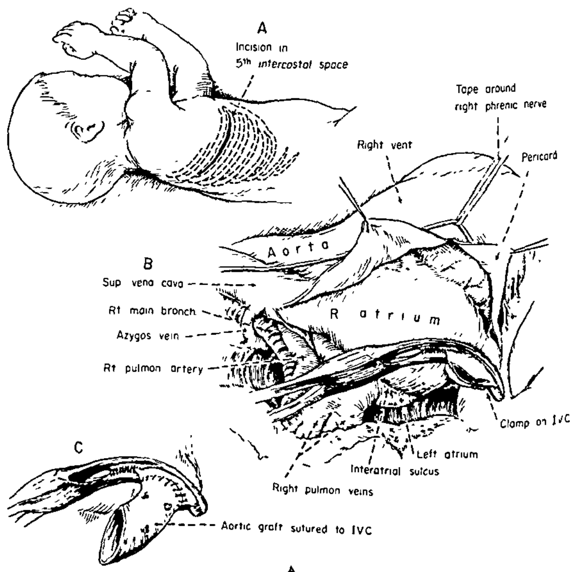
The major handicap in experimental trials was the disheartening incidence of atrial thrombosis. Among the most encouraging clinical efforts have been those of Braunwald et al. (1960), employing a fabric valve simulating the natural one, and that of Starr and Edwards with a plastic shielded ball valve. Julian et al. reported patients from their group of cases having mitral valve surgery with cardiopulmonary bypass in whom plication of the tricuspid valve annulus was also performed for tricuspid insufficiency. The mitral valve was approached through the septum, and the stenosis corrected, either by incision of the commissures or by annular plication.

In view of the rapid advances in this field, the use of statistics and specific mortality rates as related to the over-all experience of the various clinics has limited value. However, there have been a few comprehensive reports of over-all experience which have proved to be valuable sources of information.

The general considerations relating to postoperative management have been described by Sanger et al.; Effler et al. (1958); Cartwright, Magovern; and others.

COMPLICATIONS ASSOCIATED WITH EXTRACORPOREAL CIRCULATION

Acidosis. In the early clinical perfusions, during which relatively low rates were employed, metabolic acidosis was observed rather frequently. Comparative experimental and clinical studies with varying flow rates soon established that this alteration was related primarily to tissue hypoxia. With increasing modification of pump-oxygenator equipment, it has not been difficult to deliver to the patient a flow ap-



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certain undesirable effects, such as troublesome hemorrhage and hypotension, protamine titration has been employed by some.

Late Complications. The usual complications observed with major thoracic surgery and cardiac surgery have been encountered, such as pleural effusion, pericardial tamponade and pericarditis, and "postcommissurotomy syndrome." The sudden death related to low cardiac output has been previously mentioned. Kreel et al described a *perfusion syndrome*, characterized by anemia, leucocytosis, hematuria, albuminuria, fever, and occasionally by gastrointestinal bleeding. A somewhat different "perfusion syndrome" has been described by Maloney et al, who believed it attributable to microbubbles. This was characterized by areflexia, hypotension, confusion, and restlessness. This was observed mostly with bubble oxygenators and was rare with a filming type of oxygenator.

One of the most serious complications has been *infection*, particularly if extending to involve intracardiac patches of foreign material. The most effective means of managing this complication is reoperation and removal of the infected patch. Another troublesome chronic infection is that involving the sternum. Adequate drainage, including curettage, and treatment with antibiotic agents are usually effective.

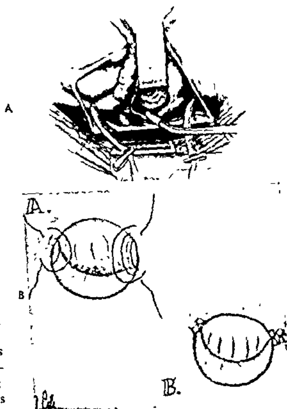


Fig. 6-123. A. Exposure of the mitral valve by the right approach is easily afforded by an incision into the left atrium along the posterior interatrial groove. (*Courtesy of Ethicon, Inc., Somerville, N.J.*) B. In mitral insufficiency with annular dilatation or contracture of the cusp adjacent to the annulus, proper closure may be achieved by shortening the annulus by mattress sutures. (*Courtesy of Kay et al. Surgery, 1961.*)

CONCLUSION

This review of clinical experience with open-heart surgery has by necessity omitted a detailed discussion of many important aspects, as well as recognition of many who have contributed materially to this field of surgery. The extension of hypothermia to profound levels by Sealy and his associates (1958), Rush et al, and others promises further extension in the time of total cardiopulmonary bypass associated with periods of total circulatory standstill. The continuous reporting of experimental surgical methods applicable to cardiac and valvular lesions, as yet not adequately correctable, is encouraging. Continued development and modification of the pump-oxygenator and surgical instruments are further means of prolonging the period of cardiopulmonary bypass. Exciting new technologic changes in the production of *prosthetic valves* and basic advances in the field of *heart transplantation* herald additional chapters to be written in this newest, most dramatic, and rapidly advancing field of surgery.

c
d
e
Compressed Ivalon sponge
b
V.S.D.
Aneurysm
a
f

Subcl. a.
Sup v cava
Aorta
Cardiac venous sucker
Caval cannulae
Fistula
Tricuspid valve
Coronary sinus orifice
Inf v cava
A

Aorta
R.A.
L.V.
B
Suture through edges of fistula including membranous ventricular septum
C
Ivalon sponge

more than a partial repair was a crucial weakness of many of the earlier operations. Though the techniques worked experimentally, they were not adequate for the larger, more complex anomalies found clinically.

Several other blind techniques were described, none of which achieved clinical status. Using three cleverly placed sutures, Martin and Essex pulled a piece of *vein-covered polyethylene* into the right atrium and over the defect. Later Donald and associates (1953) modified this technique to bring a piece of *pericardial-covered polyvinyl sponge* into the atrium and over the defect. At the same time, Kirklin and associates were using a *pericardial-covered bolus of fat* to plug experimental defects.

Earlier, in an attempt to bring the septum actually into view, Dodrill used a special, large ring clamp designed so that the clamp, in closing, brought two rings together over the atria. When the clamp was closed, the septal defect was isolated within the rings, and a small incision could then be made in the atrial wall, within the ring, to expose the defect. Unfortunately, the rings could not be made sufficiently large without occluding cardiac inflow.

Closed techniques that have achieved practical usefulness have depended upon a guiding intracardiac finger. With a finger touching the edges of the defect, the surgeon can tell approximately where to place repair stitches. Perhaps the most imaginative of these techniques is that of Gross et al., in which a *funnel-shaped cuff of rubber* is sewn to the edges of an incision in the right atrium. When this cuff is allowed to fill with blood from the right atrium, the blood rises only a few centimeters, equal to the right atrial pressure, and the surgeon can work through this well of blood to repair the defect. Kirklin and his associates (McGoon et al., 1959b) have employed Gross's technique with impressive success, often using *Ivalon patches* to close the defect. In his early use of the *atrial well*, Gross tried to close some defects with the plastic snap button devised

with an *"atrioseptopexy."* The atrioseptopexy appears to be a variation of Cohn's operation with the addition of an index finger introduced through the right atrial appendage to guide the stitch, which brings a part of the right atrial wall down to the edges of the defect. Since the right atrium is large in this disease, in most cases there is sufficient wall for such a repair. The atrial wall used in the repair was not detached from the remainder of the atrial wall, as Cohn had originally suggested.

Some time after the operations of Gross and of Bailey had been widely employed, still another operation that permitted closed repair was advocated. Sondergaard and associates (1955, 1957) placed a *circumferential suture* around the defect in the plane of the septum, and closed or almost closed the defect by tightening this suture. An important step was the opening of a dissection plane anterior to the right pulmonary veins, between the right and left atria. This technique is a direct derivation of Murray's technique, it doubtless represents an improvement, but it still cannot compete with techniques that allow careful open repair of the defect under direct vision.

While these various closed operations appeared and proliferated, some of their originators and others were working with systems to permit open-heart operations. Though not all investigators agreed, it was clear to many that a method allowing the surgeon to see the defect in a bloodless field would be better than any of the blind techniques. The *pump-oxygenator* was a logical answer, and following Gibbon's original work, a few other investigators explored this method. In 1951 Dennis attempted to close an atrial septal defect with a pump-oxygenator, but failed. It was not until 1953 that Gibbon succeeded in repairing an atrial septal defect employing extracorporeal circulation with the pump-oxygenator. Subsequently, many others have repeated this success, but between the first attempt with a pump-oxygenator and success with this device, another technique for open-heart surgery, which has been used by many surgeons in the repair of atrial septal defects, came into prominence.

Bigelow (1950a) and Boerema independently used *hypothermia* to carry out experimental open intracardiac surgery. They demonstrated that the reduced metabolic rate resulting from moderate degrees of hypothermia allowed them to interrupt cardiac inflow, by occluding the venae cavae, for a much longer time than was possible at normal body temperature. During caval occlusion, cardiotomy disclosed empty chambers suitable for open

Use of the *electroencephalogram* is helpful in determining central nervous system damage from hypoxia or embolization, but the degree of damage is not completely correlated with the changes of the electroencephalogram.

Kirklin has described a case in which a normal encephalogram was noted throughout surgery but the patient died in the immediate postoperative period and showed cerebral edema. The author had two patients with absence of encephalographic activity resulting from air embolization who subsequently recovered completely. Kirklin and others have called attention to the possible source of gas embolization resulting from the release of dissolved oxygen in the blood when it is subjected to lower oxygen tensions and higher temperatures in the body.

In operations on the mitral valve and with common atria or other instances where the possibility of air embolization is great, flooding the operative field with carbon dioxide gas has been suggested.

Hemorrhage. Significant postoperative difficulties have been encountered as a result of blood loss ascribable to various causes. Fortunately, an infrequent cause is incompatibility

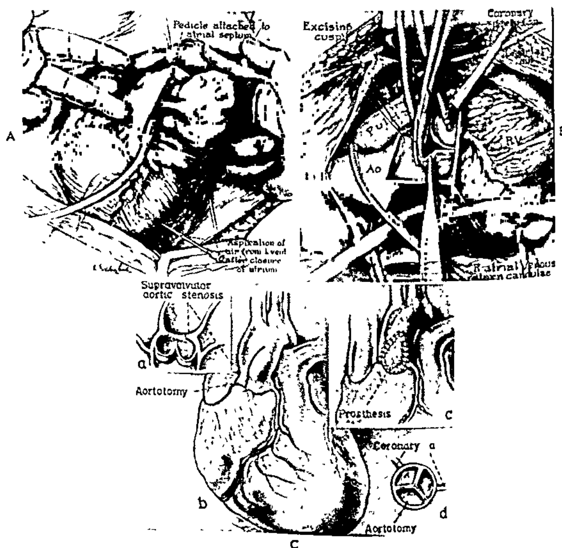


Fig. 6-120. A. Removal of pedunculated left atrial myxoma, with cardiopulmonary bypass. A vent was inserted into the apex of the left ventricle to remove residual air. (*Courtesy of Bahnson et al. Ann. Surg.* 1957.) B. Exposure of aortic valve by median sternotomy and aortotomy. Coronary perfusion cannulas and left atrial venting catheter. A fused commissure may be opened by sharp dissection or the cusp may be removed by this approach. (*Courtesy of Bahnson et al. Ann. Surg.* 1960.) C. Supravalvular aortic stenosis which does not involve the actual cusps *a* may be corrected by aortotomy *b* and insertion of an elliptical Ivalon patch to increase the diameter of the aorta. (*Courtesy of McGoon et al. J. Thoracic & Cardiovascular Surg.* 1961.)

... truly bloodless, and the technique

...

...ual blood donors. Time limitation is its most ... portant disadvantage, therefore, accurate diagnosis is required

Preoperative preparation is similar to that for any other type of heart surgery. Edema must be treated vigorously *when it exists*, but digitalization and diuretics are not used routinely.

During cooling the patient must be quiet, with-

...

... rise (Bigelow et al, 1950a), therefore, enough anesthesia is given to eliminate muscular action. A slight tightening of the pectoralis *major muscles* is an early sign of shivering and an indication for deeper anesthesia or the use of a muscle relaxant. The author and his associates have used pentothal plus Flaxedil (gallamine triethiodide) or Anectine (*succinylcholine chloride*). *Thus*, total relaxation is maintained until after completion of the intracardiac procedure, but shivering is welcomed during the warm-up period.

An automatic respirator with a semi-open system *is used to administer* 5 per cent carbon dioxide in oxygen during the cooling period and the early part of rewarming With a constant minute respiratory volume maintained throughout, the patient is actually hyperventilated at the lower temperature levels, but use of the carbon dioxide mixture prevents a dangerous rise in blood pH at the lower temperatures As an alternative, pH could be con*trolled by decreasing the respiratory* volume as the temperature falls, but this technique is more difficult and uncertain, particularly after the chest has been opened The respiratory system employing 5 per cent carbon dioxide and a constant respiratory rate and volume is preferable.

Following anesthetic induction and intratracheal intubation, electrocardiograph limb leads are at*tached to subcutaneous needles*, a polyethylene tube is inserted into the radial artery for blood pressure measurement, an electrical thermometer is placed in the rectum or esophagus, and cooling is started Refrigeration blankets at about 25°C are wrapped around the patient, and an intragastric cooling balloon or tube is inserted Gastric cooling (Holt et al, 1958) is a recent addition to the *technique, it speeds up* both cooling and rewarming in a convenient manner. In contrast to surface cooling, central cooling does not result in shivering. For each patient, a temperature graph is made, from it can be estimated the time to stop cooling in order to reach a level of 28 to 30°C *during the* intracardiac procedure Usually cooling is stopped when the rectal temperature reaches 33°C.

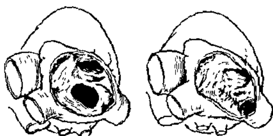


Fig. 6-125. *Repair of the foramen ovale type of atrial septal defect. A continuous suture is used first; reinforcing interrupted stitches are added.*

The electrocardiographic pattern is continuously monitored through an oscilloscope. If ventricular extrasystoles or ventricular tachycardia occurs, 100 mg procaine amide is administered intravenously, *repeatedly if necessary.*

The chest is opened either with an anterior transverse incision through the 4th intercostal spaces, or with a longitudinal incision dividing the entire sternum The author has also used a right posterolateral incision for this operation, but prefers the anterior approach

After the pericardium has been opened, the venae cavae and lung roots are encircled with *twill tape*, and the heart is explored with a finger inserted through the right atrial appendage. Thus armed with knowledge of the pathologic anatomy, the surgeon can plan his repair in detail before the *open cardiotomy. Once preparations are completed*, cardiac inflow is occluded by tightening the caval loops, and outflow is occluded by closing a clamp, one arm of which is in the transverse sinus. The right atrium is then widely opened and the right *heart is cleared of blood with suction. Because of* his previous finger exploration, the surgeon now needs only a brief inspection of the defect in the bloodless heart before the repair commences. In the foramen ovale, repair starts at the lower end near the inferior vena *cava* with a *continuous* stitch of 2-0 silk (Fig 6-125). Closure is straightforward Before this stitch is tightened and tied, however, the left atrium is flooded with saline solution to wash out air bubbles. Two or three interrupted stitches reinforce the continuous suture, and then the right atrium is filled with blood through release of the tape occluding the inferior vena cava. The atrial wound is closed with a clamp, thus allowing for a prompt restoration of the circulation The remaining caval and *outflow* occlusion is released, and, when the heart is beating effectively, the atrial wound is repaired and its *clamp removed*

In rare cases, when 8 min does not allow sufficient time, a second period of occlusion *has been*

of blood employed in the priming of the oxygenator. Another cause that has been mentioned is marked *hypovolemia* of the small patient at the end of perfusion, either through unreplaced blood loss during operation or through excessive blood return to the pump-oxygenator. As already mentioned, safety devices and maneuvers have been described, as well as various flowmeters aimed at the maintenance of a balanced perfusion.

One problem of a surgical nature is the failure to control major sources of bleeding. Postoperative bleeding with fatal consequences has perhaps been most common either through a patch employed in the right ventricular outflow tract, or from a divided coronary artery that was not secured adequately at the time of ventriculotomy.

Alterations in the clotting mechanism have been described previously, but some comments should be made here relative to neutralization of *heparin*. The earliest agent, *protamine sulfate,* has been used in a dosage up to 2 mg for each milligram of heparin given and still enjoys wide popularity. More recently, Polybrene has been employed satisfactorily and, according to some studies, more effectively. Since protamine sulfate, if given in excess, may exert

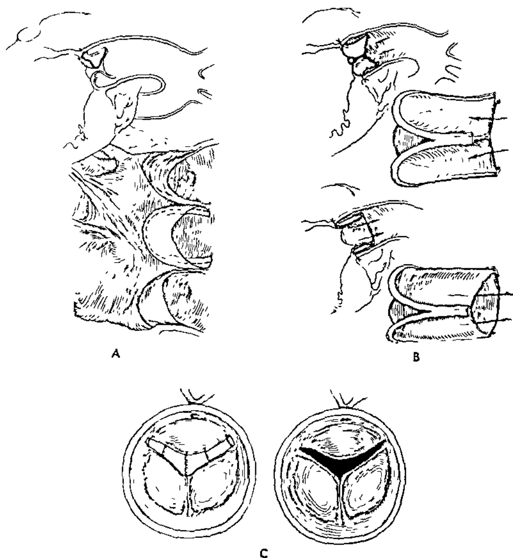


Fig. 6-122. A. For correction of aortic insufficiency involving primarily one cusp, a prosthetic cusp may be sutured in the position of the excised aortic cusp. B. In some patients, replacement of all the cusps has been necessary. (Courtesy of Hufnagel. Ann. Surg. 1959.) C. Aortic insufficiency has also been corrected by a leaflet-extension procedure. A tailored piece of synthetic material is sutured to the free edge of the contracted aortic leaflet (Courtesy of Hufnagel. Ann. Surg. 1959.)

(Fig. 6-127); the high defect may be closed in more than one way, depending upon the size of the superior vena cava and how far up the cava the anomalous pulmonary veins enter (Lewis, 1958). If the veins enter the vena cava near the atrium, the line of suture that closes the defect may simply be carried up beyond the entrance of the anomalous veins, thus dividing the lower part of the vena cava into two channels, as shown in Fig 6-126b. If the anomalous veins enter a small vena cava, such a repair would be likely to produce thrombosis of the anomalous veins, the vena cava, or both. As an alternative, the highest anomalous vein may be left undisturbed while the defect is closed (Fig 6-126c). There will still be a small left-to-right shunt after such a repair, but this is better than tying off the vein or attempting to anastomose the vein to the left atrium. As another alternative, the defect may be repaired so that the superior vena cava with its anomalous veins is directed into the left atrium, the vena cava is then divided above the anomalous veins and anastomosed to the right atrium (Fig 6-126d)

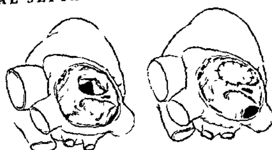


Fig. 6-127. Repair of the persistent ostium primum defect. After the notch in the mitral valve has been closed with stitches (not shown), the defect is repaired with a patch of Ivalon or Teflon.

Mitral valve disease may be associated with the atrial septal defect. The aortic leaflet of the mitral valve is notched in all cases of persistent ostium primum defect, and rheumatic disease of the mitral valve may occur with any of the atrial septal defects. The rheumatic mitral stenosis is not so severe as isolated mitral stenosis usually is in patients coming to surgery Correction of these valve deformities is not entirely satisfactory, since there may be some residual deformity, but interrupted stitches are used to close the notch in the persistent ostium primum defect, and a stenosed valve is opened with a finger inserted through the atrial septal defect before the open cardiotomy.

RESULTS

The results of surgery for these defects, particularly for the foramen ovale and high defects, have been good. There have been a number of reports with a low mortality rate and a high percentage of successful repairs. As an example, the author and his associates reported on 63 patients subjected to surgery with 6 deaths At the time of the report, 19 consecutive operations had been performed without a death, suggesting that the risk of surgery had become quite low. Others have done as well or better (Blount et al, McGoon et al., 1959b).

Evidence obtained by cardiac catheterization postoperatively has shown that the defects remain closed. Among 30 of the early patients undergoing surgery, there was evidence of a remaining shunt in only 2. One of these patients has a high defect with an anomalous vein which had been missed, and the other patient had a persistent ostium primum defect.

The *persistent ostium primum* is more difficult to close than the foramen ovale defect. Because it is near the bundle of His and the ventricular septum, drawing in of the edges during repair may cause a disrupting strain or an injury resulting in complete AV block. In addition, the notch in the mitral valve must be repaired to get a good result. Nevertheless, repair may be carried out in this defect with a relatively low operative risk, as has been impressively demonstrated by the report of McGoon and associates. They had only 2 operative deaths among 32 patients with this defect—a defect which they designated as a partial form of AV canal. Follow-up was not reported in sufficient detail to show how many of the survivors had had a satisfactory repair.

17

Surgery of atrial septal defects

F. JOHN LEWIS

INTRODUCTION AND HISTORY

Effective surgery for atrial septal defects is a triumph of the Laboratory of Experimental Surgery at the Northwestern University Medical School Exposure of the interior of the heart was required, and techniques that permit this exposure were evolved in the laboratory. The repair itself is not difficult, and once the surgeon can safely see these defects for the needed working time, he can firmly repair most of them. Exposure techniques, such as hypothermia or extracorporeal bypass, are complex, however, and they have succeeded only as the result of painstaking laboratory development The process of developing and refining continues in the laboratory, but even now, "open" intracardiac surgery dominates in the surgical repair of cardiac malformations. *Open-heart surgery* is still not the universal practice for atrial septal defects, however. *"Closed" techniques*, which played an important part in the history of this type of surgery, are still used by some.

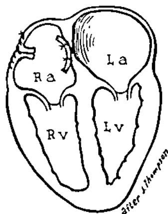


Fig. 6-124. Early experimental technique for closing atrial septal defect. A detached piece of atrial wall has been stitched down with two sutures. (From Cohn, 1947.)

The history of surgery for atrial septal defects is short but records several ingenious schemes. The apparent solution—that of bypassing the heart with extracorporeal circulation while the repair is made—has only recently come into use. The first attempts allowed repair in the blood-filled, working heart, either by completely "blind" techniques or by "blind" techniques in which touch with a finger in the heart aided the surgeon.

Cohn (1947) made the first experimental trials with a technique in which the right atrial wall was stitched down to an experimentally produced defect, using two sutures. This infolded bit of atrial wall was then cut free of the remaining wall with a wire snare (Fig 6-124). The operation succeeded in dogs, but this success might be attributed to the spontaneous healing that tends to close artificial atrial septal defects. The technique was not reliable enough for clinical use It stimulated the interest of surgeons, nevertheless, and soon a number of other techniques appeared.

Murray, employing a careful surface anatomic localization, attempted to pass sutures parallel to and through the septum itself to close either atrial or ventricular septal defects A complete closure of a septal defect could probably not be obtained in this way. Nor could the technique described by Swan (1950) for inversion of both auricular appendages through the defect be expected to result in a tight repair of the hole. This failure to achieve

PART 7

Rheumatic fever and rheumatic heart disease

intracardiac surgery. This was a sensible method for the open repair of a relatively simple intracardiac defect, such as the *foramen ovale* type of atrial septal defect; Taufic and the author (1952) accomplished such a repair with hypothermia. Presently, Cookson and associates also succeeded, and following this, Swan et al (1955) employed the method. Subsequently, the usefulness of hypothermia was somewhat extended by adding coronary perfusion during the period of inflow occlusion (Shumway et al).

The past few years have seen a decreasing use of closed techniques, an increasing use of pump-oxygenators in closing these defects, particularly the more complicated ones, and probably some decrease in the use of hypothermia, however, all three techniques are still in use at the present time (1962).

INDICATIONS FOR SURGERY

Surgery is safe enough now to be indicated for nearly all patients with uncomplicated foramen ovale. Thus, with regard to this defect, surgery has almost reached the position it holds in the treatment of patent ductus arteriosus. As in patent ductus, however, when pulmonary hypertension supervenes, indications are less definite. If the shunt has reversed and the patient is cyanotic, operation is not indicated at the present time, but just what degree of pulmonary hypertension contraindicates surgery is not easy to define The risk is higher when the pulmonary systolic pressure rises above 80 or 90 mm Hg Even pressures this high do not make the disease inoperable, however, for patients with high pressure may survive repair of the defect, and this repair offers them their best hope of continued survival Though McGoon and associates (1959b) report that the mortality rate was 53 per cent in patients with pulmonary systolic pressure above 75 mm Hg, the author and his associates (1957) had only one death in five patients with pressures over 80 One of the survivors had a pulmonary systolic pressure of 80 preoperatively, which had fallen to 34 a year after repair, because of a reduction in pulmonary artery resistance. Such reduction is evidence that the changes in the lung vessels may be reversible. For patients with partially reversing shunts, the author and his associates have devised a technique that produces slow closure of the defect over a period of days or weeks following surgery (Benjamin et al.), but this method has not as yet received an adequate clinical testing.

Also increasing the risk of surgery is *age*. The older patient with a very large heart and a history of heart failure does not tolerate surgery as well as the young asymptomatic patient. Patients should have surgery while they are still young, preferably before the age of 20. Nevertheless, older patients are still candidates for surgery if they have symptoms The author has successfully operated upon a 64-year-old woman.

The risk is slightly greater for patients with *high defects* than for those with a *foramen ovale,* and is definitely greater for those with *persistent ostium primum.* Therefore, it is helpful to differentiate persistent ostium primum preoperatively, this can be done in almost all instances. Differentiation of a high defect is not so important, as surgical indications are the same for it as for the foramen ovale. Patients with the persistent ostium primum defect need surgery too, but since the operative technique to be employed is different, preoperative diagnosis is valuable.

The *AV canal defect,* a primitive type of the persistent ostium primum, is not presently repairable. It probably should not be classified with atrial septal defects because a ventricular septal defect and a severe valvular deformity are present in addition to the atrial septal defect. In any case, it can be differentiated from the simpler atrial septal defects in most instances

TECHNIQUE

The only techniques used by the author have been open techniques with direct vision of the defect Therefore, this description will be limited to such methods The main closed techniques are briefly mentioned in the introductory section.

Since most atrial septal defects can be repaired satisfactorily with hypothermia and inflow occlusion, this method will be described first. For some defects, particularly the persistent ostium primum type or those in which the diagnosis is uncertain repair should be done with extracorporeal circulation, this method will be described further on

Hypothermia. Moderate hypothermia at 28 to 30°C permits safe open repair of the foramen ovale. The author has used this method for over 7 years. Hypothermia has several advantages, the

7

The streptococci

HUTTON D. SLADE

INTRODUCTION

The streptococci are a family of microorganisms, widely distributed in nature, composed of both pathogenic and saprophytic types. The group A hemolytic streptococci, which constitute the majority of the pathogenic types, are among the most important pathogens of man. The body of the human is the normal habitat of these microorganisms. From this reservoir the streptococci are spread by direct and indirect contact. Respiratory diseases and their manifestations due to streptococci provide a major public health problem of great economic significance. The following discussion will be largely devoted to the group A hemolytic types.

CULTURAL IDENTIFICATION

The differentiation of bacteria into genera and species by means of a group of characters is usually a difficult procedure. The streptococci are well known in this respect, although those varieties which are usually found in human and animal disease can be fairly well identified by a combination of cultural and immunological methods.

The streptococci grow in chains, are 0.7 to 1.0 μ in diameter, nonmotile, and stain gram-positive. In Fig. 7-1, the cell wall is visible as the opaque material surrounding the dense inner protoplasm of the cell. The protoplasm is confined within a smooth protoplasmic membrane. The pathogenic varieties of streptococci require, both for growth and maintenance of virulence, the addition of blood or serum to an infusion of muscle tissue, usually heart. All pathogenic strains are insoluble in bile. Many strains form capsules, are facultative (use combined oxygen for growth), and do not liquefy gelatin. The composition of a medium which will support the repeated subcultivation of group A hemolytic streptococci from small inocula is a complex one. In addition to vitamins (nicotinic acid, pyridoxal, pantothenic acid, thiamine, and riboflavin), glucose, purine-pyrimidine bases, inorganic salts and 16 amino acids, crystalline ovalbumin containing free sulfhydryl groups is required (Slade and Slamp, 1955). Growth in this de-



Fig. 7-1. Electron micrograph of Streptococcus pyogenes (group A). Shadowed with chromium at approximately 15°. (Slade, J. Gen. Phys)

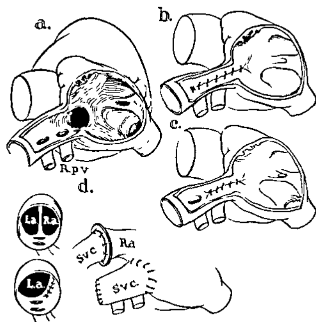


Fig. 6-126. Repair of the high type of atrial septal defect. Three alternatives are possible in order to manage the anomalous pulmonary veins In b the *suture line divides the vena cava into two channels.* In c the highest anomalous vein has been left undisturbed. In d the lower part of the vena cava with the anomalous veins has been directed into the left atrium and the proximal vena cava then anastomosed to the right atrium with a ring support.

used, but a recovery interval of 5 to 10 min should precede the second cardiac entry Occasionally, if the beat is weak as circulation is resumed, *massage* is needed for a few beats, or for a longer period if *ventricular fibrillation* occurs This arrhythmia is not likely to occur with the described technique if the heart is handled with care The author has encountered it only twice in the last 40 cases of foramen ovale or high defect, earlier, before the respirator employing 5 per cent carbon dioxide was used, reversible ventricular fibrillation occurred in about one-third of the operations

Rewarming is commenced even before the open cardiotomy, because there is a lag interval between the start of surface warming and a rise in central body temperature. With the combined use of surface and intragastric warming, both at 45°C, body temperature will be going up rapidly by the time the chest incision has been closed At 35°C warming is discontinued. *Postoperative care* may be troublesome, but this is not unusual for a patient undergoing open-heart surgery. There is some danger of bleeding in the early postoperative period and *atelectasis* may occur during the first few days

Variations in this technique have aimed at lengthening of the permissible open cardiotomy time. Both *coronary perfusion* during inflow occlusion (Shumway et al.) and *deeper hypothermia* have been used. These modifications allow some lengthening of the time for an open cardiotomy, but if the defect is complicated and much additional time is needed, the more complicated technique of *extracorporeal circulation* is needed. Hypothermia without adjuvant measures is adequate for surgery on foramen ovale defects and for high defects with partial anomalous pulmonary venous drainage Extracorporeal circulation with a *pump-oxygenator* provides the best way of operating on the persistent ostium primum defects. For the atrioventricular canal defect, there is no good repair technique.

Extracorporeal Circulation. A pump-oxygenator provides the time needed to repair the persistent ostium primum defects with a patch of prosthetic material, such as Ivalon sponge or Teflon fabric. McGoon, DuShane, and Kirklin have demonstrated the need for this type of repair in the persistent ostium primum defect. A simple closure with a line of suture is likely to result in *complete heart block* or in a postoperative breakdown of the repair. Both these end results have been observed by the author.

For open-heart operations with extracorporeal circulation, the surgeon has a wide range of choice in machinery and specific techniques. Currently the author favors a system, used by many, that employs *a Kay-Cross disk oxygenator and a DeBakey pump.*

The superior and inferior venae cavae may be cannulated with one catheter introduced at the junction of the right and left brachiocephalic veins, in order to avoid obstruction of the operating field, or each vena cava may be cannulated with its own catheter introduced through the atrium. Blood flows by gravity into the oxygenator, and the oxygenated blood is pumped back into the femoral artery with a semiautomatic pump, which is controlled by a detector sensitive to the blood level in the oxygenator A quiet, bloodless heart is obtained by occluding the ascending aorta, and its metabolic rate is slowed by flooding the pericardial sac with ice-cold saline solution.

The repairs used in the main types of atrial septal defects (Lewis et al., 1955) are illustrated in Figs. 6-125 to 6-127. Even when large, the foramen ovale defect is closed with a simple row of continuous suture enforced with interrupted stitches; the persistent ostium primum defect is best repaired with a patch

1

The streptococci

HUTTON D. SLADE

INTRODUCTION

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Fig. 7-1. Electron micrograph of *Streptococcus pyogenes* (group A). Shadowed with chromium at approximately 15°. (*Slade J. Gen. Phys*)

Table 7-1 lists the cultural properties most useful for identification purposes of the main groups of streptococci. The hemolytic group has been further divided on the basis of serologic properties. A combination of the reactions in trehalose, sorbitol, and hippurate, resistance to 60°C, and hemolysis on blood agar usually provide a presumptive identification of the streptococcus in question. Serologic methods should always be employed before the identification is considered final.

ANTIGENIC STRUCTURE

The *hemolytic streptococci* possess antigens which allow them to be classified in groups and in types within a group. These antigens may be either protein or polysaccharide in nature. Most of our information has been obtained on strains from human sources.

Grouping Antigens. The presence of polysaccharide antigens has allowed the hemolytic streptococci to be broken down into 13 groups (Lancefield, 1928). Most strains from infections in man belong to group A (*Streptococcus pyogenes*), those from lower animals, to groups B, C, D, etc. This division is not absolute because man may be infected with strains belonging to other groups, for example, group D is found in cystitis and wound infections, group G in genitourinary and throat infections.

Our information on the chemical structure of these group-specific polysaccharide antigens (termed C antigens) is limited. Recent information on type 28 and type 6 group A streptococci indicates that the group-specific carbohydrate antigen is a major component of the cell wall. As such, it probably serves as a structural component. The carbohydrate content of cell-wall preparations amounts to about two-thirds of the weight of the cell wall and about 6 to 10 per cent of the weight of the cell (McCarty, 1952). The remainder of the cell wall is composed of protein.

The group A antigen is composed of rhamnose and N-acetyl glucosamine linked to cellular protein (Schmidt, 1952). No other carbohydrates have been found to be present. The relative proportion of the two sugars in the cell wall is the same in each of the serologic types studied so far (1 part rhamnose to 1.6 parts glucosamine).

Animal passage of group A strains occasionally results in a loss of ability of the organism to synthesize the group specific antigen. Another rhamnose-glucosamine-protein complex, however, is synthesized to take the place of the specific antigen. The new compound is composed of the same two carbohydrates as the group-specific antigen. The relative proportion of the two sugars in the new antigen differs however (1 part rhamnose to 4 to 6 parts glucosamine) from the antigen present in the parent organism (McCarty and Lancefield, 1955). The serologic specificity of the group-specific antigen, therefore, depends on the intermolecular structure of the carbohydrate-protein complex.

The group antigens can be released from the cells by various methods such as treatment with dilute formamide at 150°C or 0.2 N hydrochloric acid at 100°C, enzymatic digestion, shaking with glass beads, and sonic oscillation. The latter procedure (Slade and Vetter, 1956), results in the formation of a cell-free extract which contains large quantities of both C antigen and rhamnose originally present in the cell wall of the streptococcal cell. A total of 11 electrophoretic components are present in each extract from strains representing 6 serologic types of group A streptococci. Strains within a serologic type and those of different serologic type can be distinguished on the basis of the quantitative nature of the electrophoretic patterns (Hess and Slade, 1955).

The possession of the group polysaccharide antigen is a more constant characteristic of a streptococcal strain than the ability to lyse blood cells. Although most group A strains produce *beta hemolysis* (Table 7-1), strains in groups B, C, and N may produce *alpha hemolysis* or be completely nonhemolytic.

Typing Antigens. The presence in the streptococcal cell of protein antigens has resulted in the identification of a number of distinct types within the various groups. Griffith (1927) established, by a slide agglutination method, the presence of 30 types of hemolytic streptococci pathogenic for man. Of these, 87 per cent belong to group A. Lancefield (1928) extracted cells with hot acid and extensively studied the antigenic composition of the extract by means of the precipitin test. The types now number 47. Types 7, 20, and 21 belong to group C, type 16 belongs to group G, and the remainder belong to group A.

antigen from the cells will also remove the M antigen No enzyme is known which can be used to remove M protein from the cell without destruction of the antigen.

The streptococcal groups other than A possess a varying number of type-specific antigens. The relatively rare occurrence of few strains pathogenic for man in these groups precludes further discussion of these types.

The presence of either of the two antigens in extracts of streptococcal cells can be determined by use of the *precipitin test* (Swift et al., 1943). For this purpose, antiserums prepared by the injection of heat-killed cells into rabbits is employed. It is difficult to obtain satisfactory anti-M serums with a majority of strains in types 4, 9, 22, and 25 Conversely, strains belonging to types 1, 2, 3, 5, 6, 12, 18, 19, 24, 29, and 30 usually give a strong precipitin reaction For the test, the acid extract of streptococcus cells (antigen) and the antiserum are mixed in 3-in capillary tubes, incubated 2 hr at 37°C and overnight in the refrigerator The quantity of precipitate formed is judged by eye

PRODUCTS OF THE METABOLISM OF GROUP A STREPTOCOCCI

Many substances have been identified as products of the streptococcal cell. These substances, whether they are extracellular materials such as toxins or enzymes or biologically active substances of an intracellular nature, are of considerable interest. Any or all of these substances may be concerned with the pathogenicity of the organism and biochemical changes associated with disease processes in the living animal Several extracellular substances are able to lyse red blood cells, with the subsequent liberation of hemoglobin into the surrounding medium (*hemolysins*)

Streptolysin O. This hemolysin is a sulfhydryl-containing protein which is active only in the reduced state It is produced by most strains of *group A streptococcus*, by *group C strains* from human sources, and by certain strains of group G The hemolysin is antigenic and stimulates the formation of antibodies in the blood stream of man and animals Under some conditions, it may possess activity similar to a leucocidin. Streptolysin O, either in the oxidized or reduced state, combines specifically with its antibody and, in such combination, is no longer hemolytic. The determination of such antibodies in the blood provides a useful clinical test (ASO) for the presence of streptococcal infection (Todd, 1939). The hemolysin is not a highly toxic agent. Large doses are required to kill mice. Death usually occurs in several minutes, or else the animals recover. Under these conditions no parenchymatous lesions can be seen. Hemoglobinuria is present in some animals. Streptolysin O induces the systolic contracture of the isolated frog heart following the second injection of the material. The first injection of the cardiotoxin serves to release an inhibitor which prevents the contracture of the organ; no inhibitor appears following the second injection (Cantoni and Bernheimer, 1945).

Streptolysin S. This hemolysin is a protein, possibly a lipoprotein, produced only by *group A streptococci*. It is mainly responsible for the lytic action of streptococci on the surface of blood agar plates. It is doubtful that a true antibody is produced *in man or animals* in response to the presence of streptolysin S. The serums of numerous animal species and man contain proteins which possess the ability to inhibit the hemolytic activity of the lysin (Humphrey, 1949; Stollerman et al., 1950). The *alpha-1* and *beta-1* lipoproteins of serum possess a strong inhibitor activity. Lecithin is also a potent inhibitor. Streptolysin S is highly toxic for laboratory animals, causing degeneration of parenchymatous organs and a laking of blood throughout the body. There is no critical dose as with lysin O.

Erythrogenic Toxin. *Group A streptococci* secrete a soluble exotoxin which produces a characteristic erythematous reaction when injected intradermally into the skin of man and animals. A diagnostic test, which is effected by the presence or absence of antitoxin in the blood stream, employs culture filtrates containing this toxin (Dick and Dick, 1924) The formation of the toxin is not peculiar to strains isolated from cases of scarlet fever or to any other streptococcal disease. Most young children react to erythrogenic toxin but acquire an active immunity in later life, usually due to streptococcal infection with or without clinical evidence. Erythrogenic toxin, when present in culture filtrates, is a heat-stable protein A temperature of 96°C for 45 min is required for its inactivation. The toxin is heat labile in the

fined medium allows the formation of the group and type-specific antigens.

The most valuable cultural test for the primary identification of streptococci is the presence or absence of *hemolysis* accompanying growth on the surface of blood agar. Although the original description (Brown, 1919) was given for colonies growing below the agar surface, most bacteriologists have found that the typical appearance is evident in most cases on surface growth. Three types of hemolysis can be differentiated—*alpha*, *beta*, and *gamma*.

The *alpha type*, typical of the *viridans group* of streptococci, is characterized by a zone of erythrocytes, green-brown in color, surrounding the colony, beyond this is a zone of clear to partial hemolysis. The identification of these colonies may require the use of low-power magnification. Colonies with a wide zone of hemolysis may be mistaken for the *beta* type, especially if the inner zone is narrow. The presence of a hemolysin cannot usually be demonstrated in broth cultures of organisms in this group.

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Characteristics	*Hemolytic streptococci*										*Viridans streptococci*	*Enterococci*	*Lactic streptococci*
Serologic group	A	B	C	E	F	G	H	K	L	M	None	D	N
Type of hemolysis	β	β, γ	β	β	β	β	β	β	β	β	α	α, β, γ	γ
Survives 60°C, 30 min	–	–	–	–	–	–	±	–	–	–	–	+	+
Grows at 10°C	–	–	–	–	–	–	–	–	–	–	–	+	+
Grows at 45°C	–	–	–	–	–	–	+	±			+	+	–
Hydrolysis of hippurate	–	+	–	–	–	–	–	–	–	–	–	–	–
Liquefaction of gelatin	–	–	–	–	–	–	–	–	–	–	–	±	–
Hydrolysis of arginine	+	+	+	+	+	+	±	–			–	+	±
Fermentation of·													
Trehalose	+	+	–	+	±	+	+	–	+	–	±	+	?
Sorbitol	–	–	±	+	–	–	–	–	±	–	–	±	–
Mannitol	–	–	–	+	–	–	–	–	–	–	–	+	±
Raffinose	–	–	–	–	–	±	+	+	±	?	–	+	±
Grows in 40% bile blood agar	–	+	–	–	–	–	–	–	–	–	±	+	+

+ most strains give positive reaction

igen from the cells will also remove the M igen No enzyme is known which can be d to remove M protein from the cell with- : destruction of the antigen

The streptococcal groups other than A pos- s a varying number of type-specific antigens. e relatively rare occurrence of few strains thogenic for man in these groups precludes rther discussion of these types.

The presence of either of the two antigens extracts of streptococcal cells can be deter- ined by use of the precipitin test (Swift et ., 1943) For this purpose, antiserums pre- ared by the injection of heat-killed cells into bbits is employed. It is difficult to obtain atisfactory anti-M serums with a majority of trains in types 4, 9, 22, and 25. Conversely, trains belonging to types 1, 2, 3, 5, 6, 12, 18, 9, 24, 29, and 30 usually give a strong pre- ipitin reaction For the test, the acid extract of streptococcus cells (antigen) and the anti- serum are mixed in 3-in capillary tubes, incu- bated 2 hr at 37°C and overnight in the re- frigerator The quantity of precipitate formed is judged by eye

PRODUCTS OF THE METABOLISM OF GROUP A STREPTOCOCCI

Many substances have been identified as products of the streptococcal cell These sub- stances, whether they are extracellular ma- terials such as toxins or enzymes or biologically active substances of an intracellular nature, are of considerable interest. Any or all of these substances may be concerned with the patho- genicity of the organism and biochemical changes associated with disease processes in the living animal Several extracellular sub- stances are able to lyse red blood cells, with the subsequent liberation of hemoglobin into the surrounding medium (hemolysins).

Streptolysin O. This hemolysin is a sulfhy dryl-containing protein which is active only in the reduced state It is produced by most strains of group A streptococcus, by group C strains from human sources, and by certain strains of group G The hemolysin is antigenic and stimulates the formation of antibodies in the blood stream of man and animals Under some conditions, it may possess activity simi- lar to a leucocidin Streptolysin O, either in the oxidized or reduced state, combines spe- cifically with its antibody and, in such com- bination, is no longer hemolytic. The deter- mination of such antibodies in the blood pro- vides a useful clinical test (ASO) for the presence of streptococcal infection (Todd, 1939). The hemolysin is not a highly toxic agent. Large doses are required to kill mice. Death usually occurs in several minutes, or else the animals recover. Under these condi- tions no parenchymatous lesions can be seen. Hemoglobinuria is present in some animals. Streptolysin O induces the systolic contracture of the isolated frog heart following the second injection of the material. The first injection of the cardiotoxin serves to release an inhibitor which prevents the contracture of the organ, no inhibitor appears following the second in- jection (Cantoni and Bernheimer, 1945).

Streptolysin S. This hemolysin is a protein, possibly a lipoprotein, produced only by group A streptococci. It is mainly responsible for the lytic action of streptococci on the surface of blood agar plates It is doubtful that a true antibody is produced in man or animals in response to the presence of streptolysin S. The serums of numerous animal species and man contain proteins which possess the ability to inhibit the hemolytic activity of the lysin (Humphrey, 1949; Stollerman et al., 1950) The alpha-1 and beta-1 lipoproteins of serum possess a strong inhibitor activity. Lecithin is also a potent inhibitor. Streptolysin S is highly toxic for laboratory animals, causing degen- eration of parenchymatous organs and a laking of blood throughout the body. There is no critical dose as with lysin O.

Erythrogenic Toxin. Group A streptococci secrete a soluble exotoxin which produces a characteristic erythematous reaction when in- jected intradermally into the skin of man and animals. A diagnostic test, which is effected by the presence or absence of antitoxin in the blood stream, employs culture filtrates contain- ing this toxin (Dick and Dick, 1924) The for- mation of the toxin is not peculiar to strains isolated from cases of scarlet fever or to any other streptococcal disease. Most young chil- dren react to erythrogenic toxin but acquire an active immunity in later life, usually due to streptococcal infection with or without clinical evidence. Erythrogenic toxin, when present in culture filtrates, is a heat-stable protein. A tem- perature of 96°C for 45 min is required for its inactivation. The toxin is heat labile in the

fined medium allows the formation of the group and type-specific antigens.

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Type of hemolysis	β	β, γ	β	β	β	β	β	β	β	β	α	α, β, γ	[illegible]
Survives 60°C, 30 min	–	–	–	–	–	–	±	–	–	–	–	+	+
Grows at 10°C	–	–	–	–	–	–	–	–	–	–	–	+	+
Grows at 45°C	–	–	–	–	–	–	+	±			+	+	–
Hydrolysis of hippurate	–	+	–	–	–	–	–	–	–	–	–	–	–
Liquefaction of gelatin	–	–	–	–	–	–	–	–	–	–	–	±	–
Hydrolysis of arginine	+	+	+	+	+	+	±	–			–	+	±
Fermentation of:													
Trehalose	+	+	–	+	±	+	+	–	+	–	±	+	?
Sorbitol	–	–	±	+	–	–	–	–	±	–	–	±	–
Mannitol	–	–	–	+	–	–	–	–	–	–	–	+	±
Raffinose	–	–	–	–	–	±	+	+	±	?	–	+	±
Grows in 40% bile blood agar	–	+	–	–	–	–	–	–	–	–	±	+	+

+ most strains give positive reaction
– most strains give negative reaction
± reaction variable from strain to strain
? insufficient data available.

of groups C and G and occasionally in strains from groups B and F. In addition to streptokinase (also called *fibrinolysin*), a factor present in all normal human plasma is required for lytic activity The plasma factor, called plasminogen, is activated by streptokinase to form the active proteolytic enzyme (*plasmin*). Plasmin brings about liquefaction of the fibrin. Streptokinase by itself is inactive The plasma factor is essential for enzyme activity. Streptokinase is heat stable, and purified preparations have been prepared by chemical methods. The material can be assayed by determining the quantity required to digest a known amount of fibrin at constant time and temperature.

Streptokinase is *antigenic*. Infection in man with strains of cocci which produce the enzyme will usually result in the formation of a specific antibody. The quantity of the latter in the blood can be determined by the inhibitory effect of the antibody on the liquefaction of fibrin. An increase in the serum titer of *antistreptokinase* (ASK) is indicative of recent streptococcal infection Strains of group A, however, vary widely in their formation of streptokinase. Consequently, the absence of an increase in antistreptokinase titer cannot be taken as an indication of the absence of streptococcal infection. Streptokinase can be used in the treatment of extravascular clotted or loculated hemorrhage not due to infection (Tillett et al., 1950) Fibrinous strands and coagulum are lysed by the enzyme. The exudations of chronic infection (sinusitis, osteomyelitis, ulcerative lesions) are aided by a combination of streptokinase and streptodornase (see below) In these cases, the bacterial population is reduced, large numbers of leucocytes appear, the exudate becomes thin and finally disappears, and healing occurs

Nucleases. *Group A streptococci* secrete into broth cultures a ribonuclease and a deoxyribonuclease (McCarty, 1948) The latter is also termed *streptodornase* Both enzymes are formed by all strains as far as is known. The ability of a strain to form either or both enzymes does not appear to be connected with other specific biologic activities of the strains examined.

Proteinase. Many strains of *group A streptococci* elaborate in broth culture a proteolytic enzyme which can destroy the M antigen (Elliott, 1945). The cocci in effect secrete an inactive enzyme precursor which becomes active under suitable reducing conditions, or when catalyzed by trypsin or by the active proteinase itself. The enzyme digests casein, gelatin, human and rabbit fibrin It is inactive in the oxidized state and can be converted to the active form by cysteine or thioglycollate. Proteinase and its precursor can be crystallized. The enzyme is antigenic and stimulates the formation of antibodies in rabbits. Very little antibody is formed in man during streptococcal infection. Strains of group A streptococci that are virulent for mice, usually do not form proteinase or its precursor. The passage through mice of strongly proteolytic strains which do not produce M antigen results in variant strains which are virulent for the mouse, produce M antigen, and have lost the ability to produce proteinase.

Hyaluronidase. In the culture filtrates of some *group A streptococci*, there is present a "spreading factor" which increases the permeability of animal skin to bacterial cells (Duran-Reynals, 1933). The spreading factor is probably the same as the enzyme hyaluronidase. This enzyme is able to hydrolyze the mucopolysaccharide component in the capsule of group A streptococci. Hyaluronic acid is the major component of the capsule. Preparations of the enzyme from various animal sources will remove the capsule from groups A and C streptococcal cells. In addition, the action of the enzyme on the hyaluronic acid of animal tissues points to a possible relationship of this enzyme to the virulence of streptococci. However, no parallelism between enzyme and virulence is evident, and there is doubt that the enzyme is of significance in this respect. The formation of hyaluronidase is known to occur only in types 4 and 22 of *group A*, whereas virulent strains occur among all serologic types. The formation of the enzyme by strains of *groups C* and *G* is common.

Glucuronidase. An enzyme which hydrolyzes the esters of β-glucuronic acid is produced by *group A streptococci*. A majority of the strains belonging to types 9 and 28 have been found to produce the enzyme. Positive strains among the other types are few in number (Williams, 1954). The relationship, if any, between the enzyme and streptococcal infection in man is unknown at the present time. It is of interest

The type specificity of group A organisms is due to the presence of *M protein* in the cells. A second protein antigen (T) which is not type specific also exists and is useful in the identification of the type. Both M and T antigens may occur together in the same strain. In a few types either one of the two may be present singly or shared by an antigen of another serologic type. In such cases the antigen or antigens present serve to identify the type. Types 10 and 12 contain the same M antigen but different T antigens. On the other hand, related T antigens are found in types 15, 17, 19, 23, 30, and 47 and in types 4, 24, 26, 28, 29, and 46.

The formation of M protein by any single strain of group A streptococcus is not a constant process. Repeated culture in media free of blood serum will usually decrease the quantity of M protein synthesized; in some cases it will cease altogether. Formation of the type-specific antigen will usually begin again after several passages in mice. Conversely, some strains continue to form M protein in significant quantity after years of culture in the laboratory in media free of blood serum. The T antigen is usually synthesized by the cell in a constant fashion

Strains of streptococci producing large amounts of M protein usually produce a matt colony while growing on blood agar, wherea those producing little or no M antigen posses a glossy colony.

Table 7-2 lists the properties of M and T antigens. It is evident that the two protein possess distinctly different properties. No in formation is available as to their chemica structure.

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Properties	*M antigen*	*T antigen*
Chemical nature	Alcohol-soluble protein *	Alcohol-insoluble protein †
Effect of proteolytic enzymes	Digested by trypsin and pepsin	Resists digestion ‡
Heating at pH 2	Resistant	Destroyed
Heating at pH 7	Stable	Stable
Specificity	Antigen for each type	Single antigen usually common t several types, occasionally ty specific
Antigenicity.	Antigenic in intact cell, poorly antigenic when extracted from cell	Antigenic in cell and in extract for
Protection	Antibodies confer immunity in animals	Antibodies not protective
Virulence . . .	Related to virulence of the organism	Not considered to be concerned wit virulence

* A preparation from a type 1 strain was free of nucleic acid, isoelectric point pH 5 3, phosphorus absen sulfur present (2 5 per cent).

† A preparation from a type 1 strain was free of nucleic acid, isoelectric point pH 4 5, inactivated b ultraviolet irradiation.

‡ In some strains and under certain conditions, trypsin will remove T antigen from cells.

probably occur, the presence of human reservoirs in many of these cases does not allow a critical evaluation of this route of transmission of the microorganism. (See reviews by Rammelkamp, 1956, and Paul, 1957.)

INFECTIONS DUE TO STREPTOCOCCI

The group A, "human" group C, occasionally groups D and G strains, the viridans streptococci, and the anaerobic streptococci are those within the complete family of streptococci which are capable of causing disease states in man Group A is by far the most significant in this respect.

The *streptococci belonging to group A* are responsible for a number of disease states in the upper and lower respiratory tract such as nasopharyngitis, sinusitis, laryngitis, tracheitis, bronchitis and bronchopneumonia; skin conditions such as *erysipelas*, infantile eczema, and impetigo contagiosa; generalized infections such as *septicemia* (usually acute), *scarlet fever*, and *puerperal fever*. In addition, *rheumatic fever, acute nephritis*, and *erythema nodosum* are known as sequelae of group A infections

Endocarditis is due to streptococci which may vary widely in virulence. The acute type of the disease is usually due to group A organisms, whereas the subacute or chronic type is often due to *viridans streptococci*.

The *anaerobic streptococci*, as well as the group A organisms, cause puerperal *fever*. The group A infections are usually of a less fulminating type Mixed infections with both types of cocci are fairly common.

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connective tissue fibers, the ground substance becomes swollen and intensely eosinophilic, resembling fibrin tinctorially. The terms *fibrinoid swelling* or "*degeneration*" *or* "*necrosis*," first used by Neumann (1896), were brought into common use by Klinge to designate this nonspecific, but highly characteristic alteration.

Although the intimate nature of *fibrinoid* is poorly understood, it has been shown that it consists mainly of a richly metachromatic acid mucopolysaccharide bound to a protein. Little is known about the protein component. *Klinge suggested* that fibrinoid represents a true degenerative change of the connective tissue, due to an allergic type of reaction. However, consensus of opinion today favors the belief that fibrinoid alteration is not *pathognomonic of any particular state.* Clark, Graef, and their associates indicated that fibrinoid formation depends on an escape of plasma into the ground substance, and Klemperer et al. proposed that fibrinoid develops upon coagulation of *the ground substance. According to Altshuler* and Angevine, it originates from the precipitation of an acid mucopolysaccharide The precipitant may be an alkaline protein freed from the necrotic tissue and possibly may result from the interaction between the tissue and the injuring agent. Using specific fluorescent antibodies, Gitlin et al have shown that fibrin is an integral component of fibrinoid material Their observations indicate that fibrin is deposited in intimate association with collagenous fibers "by the conversion of interstitial fibrinogen to fibrin in situ," presumably as a result of the tissue response to injury

As these alterations in the connective tissue occur, an *exudative inflammatory reaction* makes its appearance. It may be focal or diffuse and in general extends into the second or third week of the *disease (Talalaeff)*. The similarity of this exudative reaction to microabscesses was noted by various authors. It led Von Glahn to state that the masses of leucocytes, lymphocytes, and plasma cells are as prominent and distinctive features in the early phases of the process as the characteristic appearance of the Aschoff *nodule in the subsequent* phases. Predominance of eosinophils has been noted on occasions. Skworzoff indicated that an extensive exudative response often reflects a severe course, with rapidly fatal outcome.

In concurrence with the exudative reaction, nonspecific alterations such as vacuolization, wavy or fatty degeneration, and necrosis take place in the myofibers (Tedeschi et al.). Ruebner noted that the fibrinoid alteration of the interstitial connective tissue extends to involve the sarcolemma of the muscle fibers, and *that this results in damage* to the fibers involved.

Connective tissue injury, exudative *inflammatory* reaction, and myofiber damage unavoidably will end in tissue *fibrosis and scarring* From the point of view of disturbed function, *extensive collagenization is more* significant than the stigma of the process per se, i.e., the *Aschoff nodule* The latter appears relatively late in the course of the process (from the fifth to the sixth week) and, because of its small size and scattered distribution, is not likely to interfere to any great extent with the function of the organ. Instead, fibrosis and scarring, although repre*senting the healed phase of a nonspecific re*sponse, are the main cause of the lasting cardiac damage.

The Specific Response. The specific response becomes apparent about the fifth week after the onset of the process It is mainly characterized by an activation of the reticuloendothelial system. *In this* instance, an element of the mesenchyme, known as the *Anitschkow myocyte* or the *histiocyte of the heart muscle*, is converted into the classic *Aschoff cell.*

This cell was first detected by Goodhart (1879). However, it remained for Aschoff (1905) to establish its constant association *with the rheumatic* state. These Aschoff cells can be seen both in a scattered fashion, irregularly intermingled with other cells of the subsiding inflammatory exudate, or in groups within well-circumscribed nodules, the so-called Aschoff body The latter may be so small as to consist of a few cells only, less frequently it may be so large as to be detected by the naked eye. It can vary from plump and short to elongated or fusiform, the shape probably being determined by the tissue space available *for its* expansion (Baggenstoss).

Aschoff nodules have a *predilection* for the fibrous connective tissue which surrounds the adventitia of the medium-sized and small arteries. Klinge traced 48 rheumatic nodules by serial sections and found that only 5 were not *related to* vessel walls. The common sites of occurrence of the Aschoff body, in descending order of frequency, *are* the interventricular septum, posterior wall of the left ventricle, left

purified state. It is antigenic and stimulates the formation of antibodies which are not specific as to type within group A. Several immunologically distinct toxins have been successively identified.

M Protein (see also Typing Antigens). This intracellular protein is probably the most interesting biologically active substance produced by the *group A streptococcus.* On the basis of the following evidence, the M protein has been associated with the virulence and phagocytosis resistance of the streptococcus: (1) strains of streptococci virulent for mice usually contain M protein; (2) strains grown on artificial media show a reduction in M protein and decreased virulence for mice; (3) virulence and ability to produce M is restored by animal passage, (4) serums containing antibodies to M protect mice and monkeys against lethal doses of the type-specific streptococcus, while antibodies to other cellular components give no protection, (5) strains containing M are capable of growing in whole human blood, whereas those without M are destroyed by phagocytosis On the other hand, limited evidence suggests that other factors are concerned in the virulence of group A streptococci. Strains freshly isolated from acute human streptococcal infections may be low in virulence for mice and yet produce adequate amounts of M protein. The virulence of these strains may be increased many times by passage through mice.

It is clear that a relationship exists between the formation of M protein by a strain of streptococcus and the virulence of that strain. Although other cellular elements (besides the capsule) may be concerned in virulence, there is no evidence available to indicate that such elements do exist. It is likely that man is able to develop a type-specific immunity to streptococcal infection (Schwentker, 1952) Reinfection with the same type has rarely been reported The duration of this immunity is variable and probably depends on a number of undetermined factors. No conclusion can be drawn on the value of purified M protein or any other intracellular protein of the group A streptococcus for protection against streptococcal disease in man. Studies in this area are needed.

The Capsule. Many strains of group A streptococci are able to form capsules. The capsules are readily detected in the early hours of growth of the culture and soon disappear thereafter. The presence of blood serum in the medium aids in their formation. Hyaluronic acid is the main component of the capsule. Capsules can be detected microscopically by staining methods and, in liquid and solid media, by a characteristic appearance Nonencapsulated strains form small, white, hard opaque colonies on the surface of blood agar. Encapsulated strains, however, appear larger, translucent, and mucoid. The presence of capsules results in the formation of a "sticky" colony. This is evident when the colony is touched with a transfer needle. In tubes of broth, capsular cells grow in strands which remain suspended, while nonencapsulated cells produce a granular growth.

Animal infections by group C streptococci are dependent on the presence of capsules on the cells. Cells which have had their capsules removed by appropriate treatment are susceptible to phagocytosis. Hence virulent strains are encapsulated and avirulent strains are nonencapsulated. The relationship between the virulence and capsule formation by *group A streptococci* is not significant. The presence of capsules does give some protection against phagocytosis, but the degree of protection does not markedly affect the virulence of the organism.

ENZYMES OF GROUP A HEMOLYTIC STREPTOCOCCI

Studies on the enzymes secreted by the *group A streptococcus* have contributed greatly to our knowledge of the organism The enzymes which have attracted the greatest interest are those which cause tissue damage The possibility cannot be excluded, however, that enzymes which are responsible for chemical reactions of a limited nature may play an important role in disease processes. At present, it cannot be concluded that a direct connection exists between any of the streptococcal enzymes and any specific aspect of streptococcal disease.

Streptokinase. The liquefaction of fibrin clots by culture filtrates of streptococci was reported in 1933 (Tillett and Garner). Filtrates from *group A streptococci* are active against human and bovine fibrin but not rabbit fibrin The activity is also found in strains

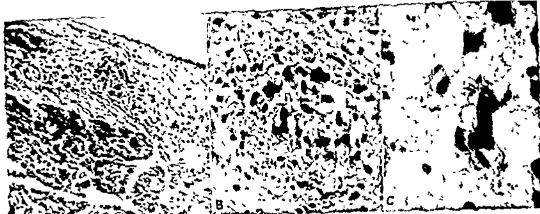


Fig. 7-2. A Early endocardial *Aschoff body.* Notice the subsiding scattered inflammatory cell infiltration and the widespread alteration of the collagenous tissue. Hematoxylin and eosin. ×175. B. Early subendocardial Aschoff body *showing* collagen alteration and incipient giant cell formation. Hematoxylin and eosin ×360 C The same Aschoff body at higher magnification displaying characteristic "owl-eyed" structures *Hematoxylin and eosin.* ×740. (From Tedeschi et al. Arch. Path. 1955.)

develop in any condition in which myofiber degeneration occurs is a *limited attempt* at regeneration

As Clawson says, the Aschoff body may represent any stage "from the active, acute exudative phase, which is less common, through the exudative *lymphocytic stage*, to the almost pure *proliferative* condition in which large mononuclear and multinucleated cells are *chiefly found*" Differences in the proportion of cell and fiber, in cellular types, and in the general arrangement of the individual constituents of the nodule may give rise to variants in the appearance of the rheumatic nodule. Gross and Ehrlich attempted to correlate the developmental sequence of tissue changes within the nodule with *the clinical course. They identified seven main histologic patterns* (large cell coronal, syncytial coronal, mosaic types, etc), all minor variants of the life cycle of the rheumatic lesion. However, the authors emphasize that some stages in the evolution of the nodule may be absent or abbreviated, or appear in reverse order, and that

TABLE 7-4 MICROSCOPIC CHARACTERISTICS OF RHEUMATIC AND NONRHEUMATIC (MYOGENIC) GIANT CELLS

	Aschoff giant cell	*Anitschkow myocyte*	*Myogenic (nonrheumatic) giant cell*
Cell border	Ragged, ill-defined	Vague, ill-defined	Sharp, clear
Cytoplasm	Basophilic	Basophilic	Eosinophilic
Nucleus	Vesicular, "owl-eyed" appearance	Vesicular, "owl-eyed" appearance	Dense, hyperchromatic
Nucleolus	Often bar-shaped	Often bar-shaped	Not seen
Number of nuclei	1 to 4	1	4 to 8
Location of nuclei	Near center of cell	Center of cell	Periphery or irregularly scattered
Striations	Absent	Absent	May be present
Location of cell	Endocardium, myocardium, pericardium	Endocardium, myocardium, pericardium	Myocardium
Toluidine blue	± to + metachromasia		
Hutter-Oleson	Dark blue		Light, pink-blue
Phosphotungstic acid hematoxylin	No striations	No striations	Striations may be present

SOURCE From Wagner and Tedeschi. Arch Path. 1955.

that glucuronic acid is a detoxifying agent in man and animals.

THE VIRIDANS STREPTOCOCCI

This group of streptococci consists of *alpha-type hemolytic strains* which are often present in the alimentary tract of man. They are consistently found in the mouth and throat. They are characterized by a failure to produce a soluble hemolysin, by the fermentation of raffinose but not mannitol, and by the failure to produce ammonia from arginine (Table 7-1).

Information on the antigenic structure of the viridans group is limited. No group-specific antigen has been identified. A carbohydrate is formed which appears to be related to that of the pneumococci The majority of the strains from human mouths and throats, and cases of bacterial endocarditis, fall into a small number of types. Some strains do not. The identity of the antigens used to establish the types in several laboratories is not clear at present. It seems likely, however, that the types in each case were recognized on the basis of a carbohydrate antigen. The pathogenicity for man and animals of the viridans streptococci is generally low, though this may vary with the strain. In no case is the virulence of these organisms considered to be high. Injection into rabbits of sufficiently large numbers of organisms may result in ulcerative endocarditis and multiple arthritis. In man these organisms are found in lesions of the teeth and gums, and they are the most frequent cause of bacterial endocarditis.

A satisfactory explanation is not available for the characteristic reactions produced by *alpha streptococci* while growing on blood agar plates. The green coloration which occurs is probably due to a reduction process The treatment of hemoglobin, methemoglobin, or laked blood with reducing agents such as ascorbic acid or cysteine results in a similar green pigment. The creation of certain environmental conditions in response to the activities of the alpha streptococci seem to be of significance as regards the two marked characteristics of these cocci: *green coloration* and *partial hemolysis of blood cells.*

THE ANAEROBIC STREPTOCOCCI

Our knowledge of these microorganisms is limited. However, many strains are pathogenic and are known to be the cause of severe puerperal infection. It is probable that the anaerobic streptococci comprise many types. Two acid-extractable antigens have been demonstrated. Only a few strains have been found to produce hemolysis in blood agar. Fermentation reactions are largely variable. The cells are about 0.3 μ in diameter. These streptococci form a part of the normal flora of the female genital tract. They have not been found in the throat or intestinal tract. In addition to puerperal infections, most of the strains have been isolated from suppurative or gangrenous lesions producing a foul odor.

EPIDEMIOLOGY OF THE GROUP A STREPTOCOCCI

The spread of streptococcal infection from its reservoir in man is closely related to the presence of human carriers. In military groups, the rate of acquisition of infection is in direct relation to the number of carriers present in a group residing in the same barrack. The upper respiratory tract, the most common site of streptococcal infection in man, is the significant source of organisms contaminating the environment Most of the cocci in the environment surrounding streptococcal carriers come from the nose rather than the throat (Hamburger et al., 1945).

Carriers vary greatly as to the ease with which they spread streptococci. This may be due to the presence of the organism in the nose and throat in low numbers and in a transient state Multiplication may also occur to produce an apparent or nonapparent infection, and these organisms may persist for long periods of time. In addition, the existence of secondary complications or nonstreptococcal infection will affect the carrier state (Wannamaker, 1954). Children seem to spread infection more easily than adults.

Group A streptococci have been isolated from the air, dust, clothing, and bedcovers in contact with carriers. These organisms are able to survive in such locations for long periods of time (Coburn and Young, 1949). The serologic types of organisms isolated from these objects correspond to the types of organisms present in the carriers in the area. However, it is not clear at this time that such objects play a significant role in the spread of streptococcal infection. Although infection by this means can

cases, extensive clinical laboratory investigation had established that the disease was inactive. Since the Aschoff body is generally regarded as the stigma of the process, the majority of investigators have selected this lesion as the yardstick of clinical-pathological correlation. In about one-third of the cases, Aschoff nodules were found in the auricular biopsy. This finding was interpreted as indicating that the rheumatic process can be active in the absence of clinical signs and symptoms

The correlation of the tissue findings with the postoperative clinical course has been also unrewarding. patients judged active histologically failed to show any increase in operative morbidity or mortality, which would have been expected had the process been active clinically (McNeely et al) Because the Aschoff body is not a static structure, consideration of its life cycle is imperative in any attempt at correlation of the clinical course and pathologic findings Selecting as evidence of activity, not the Aschoff nodule alone, but the broad spectrum of specific and nonspecific changes which are consistent with early lesion, Tedeschi and Wagner found histologic evidence of active rheumatic carditis in only 8 of 400 surgically removed auricles that they examined As in comparable series of other workers, the preoperative diagnosis in these 8 cases was chronic mitral valvular disease of rheumatic origin, extensive clinical-laboratory studies had established the process to be entirely inactive at the time of surgery Except for an elevation of the sedimentation rate in 5 cases, the postoperative course showed a striking paucity of signs and symptoms, which contrasted with the severity of the acute tissue lesions

The discrepancies between the morphologic and clinical manifestations of rheumatic activity imply that the *classic concept of acute rheumatic carditis is in need of revision* The possibility must be entertained that the widespread use of potent therapeutic agents, such as steroid hormones and antibiotics, may alter or modify the host response without affecting the underlying disease process.

Several investigators have attempted to correlate the occurrence of mural thrombosis with the various stages of the rheumatic process This approach also has been unrewarding. Some have concluded that thrombosis develops more frequently in active carditis (de la Chapelle et al.). Others noticed, on the contrary, that the incidence of thrombosis increases with the subsiding of the rheumatic process. Still others found no relation between the occurrence of thrombosis and the stage of the rheumatic process, as determined by microscopic evaluation.

The Significance of the Aschoff Nodule. The specificity of the Aschoff nodule is a highly controversial subject Since Aschoff's convincing demonstration that the lesion is pathognomonic of the rheumatic state, most investigators, including the author, have supported this view As Mallory and Keefer state, since the etiology of the disease is not conclusively established, the demonstration of the nodule is still the best evidence available on which the diagnosis of rheumatic fever can be based.

The constant association of the characteristic Aschoff nodule and rheumatic carditis acknowledges a specific response to the factor(s) causing the disease process. The bulk of direct and indirect evidence favors the concept that rheumatic fever is related in some way to a streptococcic infection. The role of the streptococcus in rheumatic fever is the one key available that promises to provide the answer to the fundamental nature of the disease Numerous investigators are pursuing the belief that hypersensitivity, or at least some form of antigen-antibody interaction, is at the root of the pathologic process Despite the attractiveness of this hypothesis, the hypersensitivity concept stands upon fragments of indirect evidence that cannot be considered conclusive. As McCarty (1948) says, "There is no information concerning the nature of the antigen-antibody system involved except for the strong implication that the antigen is probably of streptococcal origin."

This leads to the consideration of the relationship between the streptococcus and the Aschoff body per se Although it is possible that a direct relation exists between the two, none of the experimental attempts to reproduce the rheumatic lesion by means of streptococcal products has contributed a true analogue of the Aschoff nodule. Rich and Gregory have presented the closest experimental duplication of the human rheumatic lesion in rabbits sensitized with horse serum Their observations were confirmed by some investigators but could not be duplicated by others. As

Pathology

C. GEORGE TEDESCHI

BASIC ALTERATION

The term "chronic inflammation" is generally applied to disease processes characterized clinically by a relatively long duration, with or without acute exacerbations, and pathologically by a nonspecific type of tissue response, predominantly productive in character Within the spectrum of the chronic inflammatory processes, the granulomas form a special group. They are distinguished by a tissue response which is often pathognomonic of the condition that they represent, and their etiology can be established in many instances. Processes having these characteristics are therefore designated as "chronic specific."

Rheumatic heart disease is of long duration. Acute exacerbations occur, and its tissue response is predominantly productive in character. Although the etiology of the process is not conclusively established, Aschoff's demonstration (1905) that this condition is characterized by a lesion, now commonly designated as the *Aschoff nodule*, has adequately qualified rheumatic disease for membership in the "chronic-specific" group of the granulomatous inflammations.

Long before the Aschoff nodule became regarded as the pathognomonic stigma of the process, Pitcairn (1788) pointed out that the heart is frequently affected in persons subject to rheumatism. He considered that both cardiac and articular manifestations are etiologically related, a concept which had not escaped Jenner's attention (1789) However, we owe to Bouillaud the concept that the association of "diffuse articular rheumatism with fever" and "rheumatism of the serofibrous tissue of the heart" is the rule, and not an accidental combination. He further indicated that involvement of the valvular orifices is a frequent concurrent condition. Watson (1835) must be credited with the observation that rheumatic fever is essentially a disease of childhood. He noticed that the likelihood of associated cardiac and arthritic symptoms is higher before puberty than after and that it diminishes as life advances. Toward the end of the nineteenth century, laborious dissections were showing conclusively that the heart is frequently affected in rheumatic fever (Goodhart, Romberg, Poynton). It remained to the investigators of our times to demonstrate (1) that rheumatic fever is a systemic disorder of the connective tissue predominantly affecting joints and heart, but also involving other organs and structures and (2) that, in the heart, it strikes simultaneously collagen and myofibers, eliciting both a specific and a nonspecific type of response.

The Nonspecific Response. Pioneer students of rheumatic disease (Aschoff, 1905; Mallory; Huzella, and Fraenkel) clearly recorded the fact that alterations occur in the connective tissue of the heart in the early phases of the process, long before the appearance of the Aschoff nodule However, it was only in 1933 that the results of extensive work by Klinge aroused general interest in the interpretation of this early lesion. As changes in the collagenous tissue take place, the connective tissue fibers become tortuous and edematous, waxlike, refractile, and often fuse with one another. In the meshes between the altered

association of nonspecific inflammatory changes and of lesions characteristic of the rheumatic process, including *Aschoff nodules* The latter are frequently obscured by the overwhelming nonspecific response.

The exudate may become completely absorbed, with restitution and regeneration of lining mesothelial cells, or may be organized and replaced by granulation tissue, with scar formation in the later stages. The latter may appear in the form of a few fibrous plaques of no great importance, in either or both of the pericardial layers (*milk spots*). Or, they may cause dense bands, extending from the visceral and the parietal pericardium (*adhesive pericarditis*), often so numerous as to obliterate the pericardial cavity Less frequently, the inflammatory process extends to the external surface of the pericardium (*external pericarditis*) As healing occurs, the parietal pericardium becomes bound by adhesions to the mediastinum and other adjacent structures (*adhesive mediastinopericarditis*) If calcium salts precipitate in the scarred pericardial membranes, the heart may become enveloped by a solid wall of calcified fibrous tissue (*constrictive pericarditis*) Droplike cysts may be seen occasionally on the thickened and distorted pericardial surfaces (Lauche) Their formation has been traced to mesothelial cells bridging the crevices of the organized fibrinous exudate The main functional disorder resulting from constrictive pericarditis is a reduced flow of blood to the heart. Surgical dissection of the adhesions has been proposed and successfully performed

Myocarditis. The gross appearance of the myocardium in the early phases of the rheumatic process is not revealing Slight enlargement of the ventricles, particularly of the left, may be noticeable Occasionally some degrees of *myocardial hypertrophy* and thickening and lengthening of the papillary muscles are also present Since in the early phases of the disease there are no mechanical difficulties (valvular deformities, pericardial adhesions), myocardial hypertrophy may be explained on the basis that the spared muscle attempts to overcome the deficit created by the primary injury to collagen and myofibers As the process enters the granulomatous stage, pale-gray nodules of various shapes may become visible, particularly along the course of the thinnest branches of the coronary arteries They are mostly rounded or elongated, the size of a pin point, rarely larger. These are the Aschoff nodules, but they are seldom detected by the naked eye.

As the process advances, the heart undergoes prominent changes in size, shape, and structure. These changes vary greatly from case to case according to the degree of strain imposed on the individual chambers by the frequently associated valvular deformities, the amount of constriction created by the adherent pericardium, and the extent of myocardial fibrosis and scarring which represent the healed phase of the process.

Endocarditis. The appearance of tiny wartlike translucent nodules (*verrucae*) in rows or clusters, along the lines of closure of the cusps of the valves is the most characteristic alteration of rheumatic endocarditis. (Following the recommendation of Gross and Kugel, the term "cusp" is used to designate the component part, both of the semilunar and AV valves) These verrucae may vary in size from pin point to 2 or 3 mm and in color from pearl gray to tawny. As a rule, they are located on the atrial surface of the mitral and tricuspid valves and on the ventricular surface of the semilunar valves Less frequently they are seen implanted on the chordae tendineae, the papillary muscles, and the mural endocardium lining the left atrium. Since these verrucae adhere firmly to the endocardial surfaces, rarely they become dislodged and cause embolisms The affected valves are thickened, edematous, and slightly roughened, particularly at the free margins Rheumatic fever is a disease characterized by repeated recurrences, rather than by a sustained chronic inflammatory process In accordance with this belief, coexistence of verrucae in various stages of activity is not rare. Repeated attacks cause increased thickening of the valve. The rings become more prominent and indurated; the chordae tendineae become thicker, shorter, and are often fused

The valves most frequently affected are the aortic and mitral. The tricuspid and pulmonary are rarely involved. However, Gross and Friedberg have shown that lesions of microscopic dimensions can be seen in the tricuspid valve as often as in the valves of the left side of the heart.

TABLE 7-3 INCIDENCE OF ASCHOFF NODULES IN SURGICALLY REMOVED AURICULAR APPENDAGES

Author	Date	No. of cases	Incidence of Aschoff nodules	
			No.	%
Pinniger	1951	15	10	67
Waaler	1952	28	8	28
Kuschner et al.	1952	11	4	36
Sabiston and Follis	1952	43	32	74
Biorck et al.	1952	18	8	44
Janton et al.	1952	88	14	16
Kuschner et al.	1953	28	14	50
Enticknap	1953	71	29	41
Decker et al	1953	183	83	45
Thomas et al	1953	40	22	55
McKeown	1953	53	24	45
Denst et al	1954	75	21	28
Luse et al	1954	77	32	41.6
Elster et al.	1954	15	9	60
Manchester et al	1955	35	13	37.1
Tedeschi et al	1955	400	75	18.8
All cases		1,180	398	33.7

SOURCE: From Tedeschi et al Arch. Path 1955.

posterior papillary muscle, pulmonary conus, posterior wall of the left atrium, and the myocardial wedge between the aorta and the left atrium (Gross and Ehrlich) However, Clawson found them as commonly in the apex as in any other portion of the heart.

According to Gross and Ehrlich, the percentage of Aschoff nodules noted in postmortem material of different series of rheumatic hearts ranges from 32 to 94. Tissue studies on surgically removed auricular appendages indicate as broad a percentage range of frequency of occurrence (Table 7-3) Several investigators have found a high degree of correlation between the incidence of rheumatic nodules in the auricles and that of other portions of the heart. Discrepancies in the incidence of the Aschoff body are probably due largely to the nature of the sampling and to the morphologic criteria used for the identification of the nodule

The Life Cycle of the Aschoff Body. The Aschoff nodule is not a static structure. Aschoff was the first to define the ultimate transformation of the rheumatic nodule into connective tissue. The earliest detectable change in the development of the rheumatic nodule is swelling and edema of the connective tissue fibers and fibrinoid alteration of the ground substance. Polymorphonuclear leucocytes, lymphocytes, and plasma cells are usually present in varying numbers. As the lesion progresses and the exudative reaction subsides, large histiocytic cells (mobilized Anitschkow myocytes) become more and more numerous and finally dominate the picture (Fig. 7-2A, B). These cells are readily recognized by the "owl-eyed" appearance of the nucleus and by the abundant basophilic cytoplasm (Fig. 7-2C). Then a few giant often multinucleated cells, in close relation to one another and generally located in the central portion of the nodule, make their appearance. The ragged, ill-defined cell border, the basophilic cytoplasm, the vesicular "owl-eyed" appearance of the nucleus, and the often bar-shaped nucleolus give rise to a cellular structure so characteristic that it has received almost general recognition as being unique in the rheumatic process. Shortly after the structure of the Aschoff body was elucidated, a controversy arose concerning the origin of these giant cells.

Against Aschoff's original belief that they originate from mesenchymal periadventitial cells, Saigo suggested a derivation from cardiac muscle. This concept was supported by Whitman and Eastlake and denied by several other investigators, but again advocated by Murphy (1952). Observations on human postmortem material and on experimental lesions induced in rabbits led Murphy to conclude that the Aschoff giant cell represents the sarcoplasm of damaged myofibers, proliferated muscle cell nuclei, and syncytial multinucleated cell masses beneath the sarcolemma. The unequivocal demonstration of Aschoff bodies in sites utterly devoid of cardiac muscle and the clear elucidation of an evolutionary relationship between the Anitschkow myocyte and the Aschoff giant cell cast doubt for a time on the myofiber theory (Wagner and Tedeschi). This controversial point has been recently clarified by the demonstration that two types of giant cells, each provided with distinctive morphologic and histochemical characteristics, can be found in rheumatic carditis (Table 7-4). The Aschoff giant cell which is derived from the myocyte of Anitschkow is a *specific response to the primary connective tissue injury;* and the myogenic type of giant cell which may

association of nonspecific inflammatory changes and of lesions characteristic of the rheumatic process, including *Aschoff nodules*. The latter are frequently obscured by the overwhelming nonspecific response.

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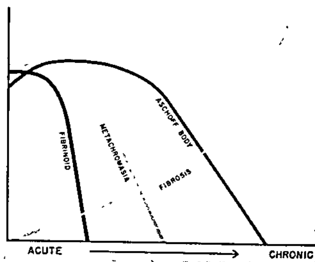


Fig. 7-3. Stages in the development of the Aschoff body.

fibrinoid cannot be demonstrated with any degree of constancy, depending on the tissue reactivity Similarly, Aschoff (1905) has made clear that "it is in no way essential that the formation of the richly cellular nodules should be preceded by fibrinoid degeneration of the ground substance"

From 3 to 6 months from the start of the process, regressive changes begin to take place. Giant cells and Anitschkow myocytes become scarce and rarely show the characteristic owl-eyed nuclei The nucleus is more often pyknotic than vesicular and in many respects resembles the "ghost nuclei" described by Gross and Ehrlich and interpreted as indicating senescent change. Fibroblasts and collagenous fibers become more numerous, and later they fuse into dense bundles of collagen As the process ages, metachromasia of the ground substance may persist for a while, owing to the accumulated acid mucopolysaccharide, in the absence of fibrinoid (Tedeschi, Wagner, and Pani). The final stage is characterized by roughly concentrically laminated nodules of scar tissue, often located in the perivascular connective tissue. This chain of events is represented in Fig. 7-3.

Reactivation of the process is accompanied by the appearance of fresh lesions This explains the possible coexistence, in the same heart, of Aschoff nodules in different stages of development and of old and recent alterations of the nonspecific tissue response

The Problem of Rheumatic Activity. In the majority of the specific granulomas, tissue healing denotes clinical quiescence of the process. This is well exemplified by the evolution of the tubercle. Morphologic patterns assumed to represent active disease are usually accompanied by clinical manifestations. With histologic evidence of diminution in the intensity of the process, clinical activity may correspondingly subside. It has not been conclusively established as yet whether or not the age of the Aschoff nodule similarly offers a basis for correlation with the stage of the disease it represents.

The clinical course of the rheumatic state is characterized by manifold signs and symptoms and lacks uniformity, furthermore, in many instances the course is silent. This is well illustrated by the natural history of the 1,000 cases of rheumatic fever of Jones and Bland, where one-third of the patients with recurrent disease had symptoms so mild that the recurrence was not detected at the time the attack occurred. Likewise, Rogers and Robbins have shown that the initial, as well as recurrent, attacks of rheumatic fever in the late years of life may proceed insidiously into cardiac failure and death, with complete absence of characteristic symptoms and signs

Any attempt at clinical-pathological correlation must be qualified by the knowledge that the organic response to the rheumatic injury reflects a complicated interaction among host, agent, and environment and that each of these three factors is per se a variable. It is, therefore, understandable why the time required for the development of the various pathologic manifestations cannot be predicted with any degree of accuracy.

Andrei and Ravenna expressed the belief that the mere presence of the Aschoff body does not imply that the process is active or has been active in the near past. Supportive evidence of this statement has been recently presented, when the development of techniques for the surgical correction of deformities of the mitral valve have made available cardiac tissue from living patients with rheumatic disease. These techniques require the removal of part or all of the left auricular appendage, and this has been made the object of extensive pathologic investigation. By this method, well over 1,000 auricles have been evaluated (Table 7-2), and the pathologic findings in the individual instances have been compared with the clinical course. In all these

uniformity in changes among the various components of the mitral valve. Harken et al. have contributed to the understanding that variations of findings must be anticipated and taken into account in any attempt at surgical correction of the deformed valve. They recognize two main anatomic groups of mitral stenosis. One type is characterized by a *rigid fibrous contraction of the leaflets* with anatomically normal chordae In the other type, *fusion of the chordae* gives rise to a funnel-shaped structure. Actually, chordae, leaflets, and commissures, either singly or combined, can be affected. This may result in chordal, cuspal, commissural, and combined types of mitral stenosis. In the 70 cases of Rusted et al, commissural stenosis was present in 22 cases, cuspal in 11, and chordal in 6, whereas in the remaining 31 cases, cusps, chordae, and commissures were involved in various combinations.

In the chordal type, shortening and fusion of the chordae pull the valvular leaflets downward and reduce their mobility, converting the valve into a funnel-shaped structure. In the cuspal type, the main cause of the stenosis is the conversion of the mitral leaflets into leathery, rigid membranes In the commissural type, the leaflets are thickened and less pliable, but the depth of the valve is not altered; or there is fusion of the valvular leaflets, and the depth of the commissure is increased (Rusted et al.). Combinations of two or three of the above-described changes include thickening of the commissures and of the free portions of the leaflets, or fusion of the valvular leaflets associated with thickening, shortening, and fusion of the chordae. Some measurements of the components of the stenotic mitral valve are here included, inasmuch as they might provide useful information to the surgeon attempting to correct the stenotic valve (Tables 7-5 to 7-7).

Of the 50 hearts examined by Rusted et al, 31 showed calcification of the valvular leaflets Cases are on record of lethal cerebral embolism caused by calcium dislodged at mitral valve commissurotomy.

It is generally assumed that, in mitral stenosis, the ring of the mitral valve is smaller than normal However, Coombs has shown that it is frequently dilated. Others (Rusted et al.) have substantiated this observation.

The pathologic changes that underlie the slow but relentless development of mitral stenosis are progressive in nature There are two main views regarding the pathogenesis of the progressive thickening of the valvular com-

TABLE 7-5 MEASUREMENTS OF COMPONENTS OF MITRAL VALVES IN MITRAL STENOSIS: 50 HEARTS

Structure	Depth, cm		Thickness, cm	
	Range	Average	Range	Average
Anterior cusp				
Thick portion	0 4-2 0	1.1	0.1-0 7	0.31
Pliable portion	0 6-2 7	1 5		
Total depth	2.0-3 5	2 6		
Posterior cusp				
Thick portion	0 0-1 4	0.8	0.1-0 65	0 27
Pliable portion	0.0-1 2	0.6		
Total depth	0 6-2 2	1.3		
Anterolateral commissure				
Thick portion	0 0-1.9	0.9	0 1-0 85	0.32
Pliable portion	0.0-1 1	0 5		
Total depth	0 5-2 5	1.3		
Posteromedial commissure				
Thick portion	0.2-1 8	0.9	0.1-0.85	0.32
Pliable portion	0 0-1 9	0 3		
Total depth	0 3-2 9	1 2		

SOURCE: From Rusted et al. Circulation 1956.

already indicated, there is no definite proof that the lesions of rheumatic fever in human beings are due to anaphylactic sensitization.

Likewise, the evidence of the role of hyaluronic acid and hyaluronidase in the pathogenesis of rheumatic fever is more tentative than conclusive. Guerra suggested that the widespread involvement of the mesenchymal tissue in rheumatic disease is due to partial removal of the protective barrier provided by the ground substance. Hyaluronidase and perhaps other enzymes might act in this way. Since fibrinoid alteration is believed to be different in the various collagen diseases, it is not unreasonable to consider the fibrinoid of the acute rheumatic state as a manifestation of streptococcal activity.

As already indicated, the Aschoff nodule is not available in every rheumatic heart to substantiate the clinical diagnosis, in many instances the main morphologic manifestation is that of a healing or healed nonspecific carditis. Inasmuch as fibrosis and scarring represent the end result of the primary collagen injury and the final phase in the evolution of the nodule, such findings do not negate the clinical diagnosis. Rather, they offer tentative support. However, lack of definitive rheumatic criteria in hearts seen at postmortem and showing single or multiple valve involvement raises the question as to whether or not these hearts can be still classified as rheumatic As stated, "If one accepts the thesis that calcific aortic stenosis may be nonrheumatic or rheumatic in origin, one might extend such reasoning to the consideration of mitral stenosis." Regardless of cause, the end results of a carditis do not differ on strict morphologic ground. The decision on the rheumatic or nonrheumatic nature of the process will mainly rest in these cases on historical and clinical data, an approach necessarily arbitrary and containing the inaccuracies inherent in the method.

Stokes and Dawber have indicated that less than half the patients with rheumatic heart disease recall clinical manifestations of rheumatic fever. In their series, only 41 per cent of the patients in whom the diagnosis was based upon auscultatory findings recalled having had rheumatic fever This varied from 54 8 per cent of those with multiple valvular involvement to 21.1 per cent of those with aortic regurgitation alone. In the absence of a positive history, it is not possible even to speculate whether the involved tissues show the healed or healing stages of rheumatic carditis or the nonspecific changes secondary to unknown causes. Consequently, the rheumatic origin of the cardiac lesion is usually based merely on the exclusion of other possible causes and on the assumption that rheumatic fever is one of the most frequent causes of heart damage.

It is obvious that other factors beside the highly suspected streptococcal injury play a role in the disease. Relatively few individuals appear to be susceptible, and only a small percentage of streptococcal infections lead to the rheumatic state.

Both genetic and endocrine factors have been held responsible for the predisposition to the disease. It has been also implied (McKusick) that a number of morphologic abnormalities of the cardiovascular system which become apparent later in life may be predicated on a congenital defect of the mesenchymal tissue. If this is true, susceptibility to the rheumatic state might also be influenced by an inborn aberration of the collagenous tissue.

PATHOLOGIC ANATOMY OF THE HEART

The alterations outlined above may involve the endocardium, the myocardium, and the pericardium, either singly or combined. Most frequently, with differences in degree, all three cardiac structures become affected (pancarditis).

Pericarditis. Pericarditis is the most common accompaniment of rheumatic fever. Friedberg and Gross have shown that microscopic involvement can be found in every instance of acute or recurrent rheumatic carditis In the acute phases of the process, the formation of an exudate occurs which is mostly *fibrinous*, less frequently *serous*, and rarely *purulent*. The fibrinous exudate can be so scanty as to appear in the form of a minute web finely deposited on the congested pericardial surfaces or so abundant as to cause clumps or masses of fibrinous material. Because the latter resembles sheep's fur, it is generally referred to as *cor villosum*. The corresponding microscopic picture is that of an

tysis and to intraparenchymatous *hemorrhages*, which *in turn will result* in extensive *hemosiderin deposits* and fibroblastic tissue proliferation (*brown induration*). Thickening and sclerosis of the walls of the capillaries and arterioles and narrowing of the lumens will interfere with the gaseous interchange. This will be restricted *further* by the fibrosis taking place in the alveolar walls, which may become *twenty times thicker* than normal. These *pulmonary* changes will place an extra burden on the right ventricle, causing dilatation of

[illegible]

At this stage of the process, failure and atrial fibrillation are likely to develop, and thrombosis of the auricle or of the atrium is frequent By this time the heart has assumed a characteristic shape, resulting from a small left ventricle, a broadened pulmonary conus, and dilated right and left atria.

MITRAL INSUFFICIENCY. *A certain degree* of valvular *insufficiency is present in almost* every instance of mitral stenosis. If valvular incompetence is the prevailing defect, the heart may become enormous. In addition to the enlargement *of the left atrium and the* right chambers of the heart, which are the *chief cardiac deformities of mitral stenosis*, the left ventricle also undergoes hypertrophy and dilatation.

Several surgical procedures have been suggested aimed at the production of a flap or sling valve which would compensate for the *mitral leak at each ventricular systole. However*, techniques applied to the surgical correction of mitral insufficiency have not yet reached the ideal stage of standardization as obtained in commissurotomy of mitral stenosis.

AORTIC STENOSIS Aortic stenosis comprises 40 per cent of all *valvular deformities* Adhesion of the cusps at the *commissures*, thickening and fibrosis of the ring and cusps, and scarring, retraction, and stiffening of the free borders well explain the frequent association of *some degree* of insufficiency.

From the time of *Monckeberg's classic* description, the frequent association of *aortic* stenosis with calcific nodularities on both surfaces of the cusps and in the sinuses of Valsalva is a well-recognized condition (*calcific nodular stenosis*). *However*, the nature of the lesion is still a matter of controversy. Some investigators advocate that rheumatic injury is the most frequent cause of the deformity (Hall and Ichioka; *Karsner and Koletsky*). Others have taken *into account other* etiologic factors, *including degenerative* or metabolic disorders, senescent changes, and the effect of *tension* and vibration *on* certain portions of the valve. It is apparent that, in the absence of rheumatic stigmas, *it is not* possible to speculate whether the valvular deformity represents the healed stage of rheumatic *valvulitis* or the nonspecific *tissue response secondary* to unknown causes.

Left ventricular hypertrophy, with minimal or absent dilatation, is the direct effect of the valvular deformity on the cardiac muscle. The other chambers of the heart remain unaffected until failure takes place and the right side of the heart becomes dilated. As scarring and calcification extend into the interventricular septum, *disturbances in AV conduction may occur* (Boas). *Precordial pain* may also develop (Contratto and Levine). This can be explained on the basis of increased cardiac activity or diminished blood flow in the coronary arteries (valvular stenosis or narrowing of the coronary arteries, possibly rheumatic), resulting *in myocardial ischemia*.

AORTIC INSUFFICIENCY. *Aortic insufficiency* is less well tolerated than aortic *stenosis* and is generally accompanied by the greatest degree of cardiac enlargement (1,000 Gm or more). *Left ventricular hypertrophy and dilatation* develop almost simultaneously. As the *mitral valve becomes* incompetent, first the left atrium and *then the chambers* of the right heart undergo *hypertrophy and dilatation*.

In aortic insufficiency and, to a *less extent*, aortic stenosis, areas of fibrous thickening appear in the mural endocardium of the interventricular septum of the left ventricle. This *fibrous thickening*, in the form of pockets, imitates *the form* of valve cusps.

While it is possible *that*, *in some instances*, the thickening represents the end result of a circumscribed area of mural endocarditis, it is generally believed that, in the majority of *cases*, the lesion results from irritation and undermining of the endocardium produced by the vortices of *blood flowing* to and from the distorted valve. In the *diastolic pockets of*

Early students of rheumatic endocarditis held the view that the verruca consisted of a conglomerate of platelets and fibrin, deposited on the cusp surface. They believed that this was the primary manifestation. Subsequently it was shown that, before the verruca makes its appearance, both nonspecific and specific alterations occur in the deeper structures of the cusps. The nonspecific response consists mainly of collagen degeneration and inflammatory cell infiltration; the specific response is characterized by the appearance of the Aschoff cells and nodules. The latter are most frequently found in proximity to areas showing degeneration of collagen fibers and fibrinoid alteration of the ground substance, which often extends to the valve surface. The valve rings, almost invariably affected, can show lesions even in the absence of alterations in the valve cusps. This has led Gross and Friedberg to suggest that the *annulus is probably the first portion of the valve leaflet involved by the rheumatic process.* Healing takes place through a proliferation of fibroblastic tissue and results in fibrosis, scarring, elastosis, and increased vascularity *Recurrent valvulitis* is characterized by concomitant occurrence of healed and acute lesions.

It is generally agreed that the rheumatic valvular lesion proceeds from the deeper structures of the cusps toward the endothelial surfaces and that the verruca is a subsequent manifestation However, the nature and mode of production of the basic lesion are still a matter of dispute Some workers believe that the verrucae are composed of subendothelial fibrinoid material exuded through the injured endothelial cell layers (Neumann) Others believe that they consist of disintegrated endothelial cells matted together with fibrinoid material. Still others believe that they represent accumulations of platelets and fibrin Hypertension and the ensuing mechanical trauma are important underlying factors, and this explains their most common occurrence along the line of closure of the valves.

Alterations comparable to those taking place in the valvular endocardium occur in the *mural (parietal) endocardium*, particularly in the subvalvular angles of the aortic valve, the septum fibrosum, the papillary muscles of the left ventricle, and the left atrium, where they cause a highly characteristic lesion, known as the *MacCallum patch.* This latter occurs in 29 to 80 per cent of the cases. It consists of a flat, or slightly raised, area of endocardial thickening with distinct projections resembling vegetations and low ridges and hillocks separated by furrows with no definite pattern.

The lesion may be well demarcated, or it may involve almost the entire endocardial surface, extending into the auricle and the orifices of the pulmonary veins. Auricles removed from patients with rheumatic mitral valvular disease have revealed the high rate of occurrence of endocardial fibrosis in this portion of the heart. However, Denst et al. warn against interpreting the thickened endocardium of the auricle as necessarily indicative of healed rheumatic disease, since the endocardium in this location normally is thicker than in other areas of the heart.

Valvular Deformities. A rheumatic valvulitis may heal without leaving any grossly demonstrable defect, or it may result in a gradation of permanent injuries, ranging from a hardly detectable fibrous thickening along the line of closure of the valve leaflets to a prominent valvular deformity.

Baggenstoss warned that, "caution should be exercised in the interpretation of valvular deformities" and that, in the absence of good clinical and pathologic evidence of a previous rheumatic state, "more will be gained by withholding judgment and carrying on further investigation than by arriving at more or less dogmatic conclusions"

The wisdom of this statement is supported by the knowledge that, although rheumatic fever is the main offender, a wide variety of toxic, infectious, and metabolic disorders may cause valvular damage, which may result in fibrosis and scarring. Of 73 cases of valvular deformities analyzed by Clawson et al, only 55 had a dependable history of rheumatic disease Of these, only 27 revealed pathognomonic rheumatic lesions The deformity can result in either valvular stenosis or insufficiency, or both The mitral valve is most frequently affected, followed in order of frequency by the aortic, tricuspid, and pulmonic valves

MITRAL STENOSIS. According to White, mitral stenosis and mitral regurgitation are almost invariably combined; however, one disorder can prevail over the other. There is no

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MITRAL STENOSIS. According to White, *mitral stenosis and mitral regurgitation* are almost invariably combined, however, *one* disorder can prevail over the other. There is no

and causes muscular ischemic damage and weakness.

Cardiac pain and discomfort, with anginal characteristics, have been frequently described in children and young adults affected by rheumatic heart disease. The author had the opportunity to study the hearts of three children aged 5, 9, and 13, dying of acute rheumatic pancarditis, in all of whom precordial pain had been a predominant symptom. In two cases, the anterior descending branch of the left coronary artery and, in the third, the left circumflex artery disclosed recent thrombotic occlusion of the lumen There was associated severe vasculitis It is probable that, in these three cases, the circulatory disorder contributed to the coexistent myocardial damage and that it represented an important factor in precipitating the fatal course of events

Although similar cases have been reported by others, thrombosis of the large branches of the coronary arteries is not a frequent complication of the rheumatic state. In the Karsner and Bayless series of 56 rheumatic hearts, thrombosis was noted in the smaller arteries in 6 cases, in the capillaries in 1 case, and in the veins in 14 cases, a total of 21 cases (37 per cent of the entire group).

The significance of rheumatic vasculitis as a factor predisposing to arteriosclerosis is an old debated question Zeek has advanced the view that rheumatic heart disease predisposes to early development of atheromatous lesions in the coronary arteries Wiesel and many others have shown that rheumatic coronary arteritis frequently results in a juvenile form of arteriosclerosis

Although a direct sequence of events has not been conclusively shown, it is probable that the precocious *coronary sclerosis* that follows the rheumatic state represents the healed stage of the collagen alteration and vasculitis that take place in the early phases of the process

Numerous investigators have stressed the similarity of the rheumatic vasculitis and the vascular disorder which occur in periarteritis nodosa Friedberg and Gross went so far as to express the opinion that both conditions are etiologically related Similarly, Fahr recognized a link between rheumatic arteritis and malignant sclerosis and later drew attention to the resemblance of vascular lesions in the rheumatic state, polyarteritis nodosa, and dermatomyositis. Klinge extended the relationship to include thromboangitis obliterans and focal glomerulonephritis and all the conditions which are thought to be characterized by a hyperergic type of reaction. By sensitization methods, several investigators have obtained in the experimental animal close duplication of the vascular changes of rheumatic fever; but there is no definite proof that the lesions of rheumatic fever in the human are due to anaphylactic sensitization, and one can only go so far as to say that rheumatic vasculitis shares with other conditions some of the indefinite patterns of the so-called collagen diseases.

CAUSES OF DEATH

Statistics from various sources indicate that rheumatic disease, particularly in youth, is one of the leading causes of death. Life expectancy varies with the age of onset of the disease.

Cohn and Lingg have shown that, when the disease begins early in life, 69 per cent survive childhood, 35 per cent survive the adolescent period, 18 per cent reach the age of 30, and only 5 per cent live beyond the forty-fifth year. When the disease occurs during adolescence, 85 per cent survive this age period, 55 per cent reach the thirtieth year, and 21 per cent live beyond the forty-sixth year. When the disease strikes in the third decade, 23 per cent go beyond the forty-fifth year; and when the onset occurs after the third decade, 44 per cent survive the forty-fifth year. Of the 1,000 patients with rheumatic fever followed by Jones and Bland, approximately one-fifth (203 patients) had died 10

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to be 14 7 per thousand a year, with the highest incidence between the ages of 1 and 4 years (33 2 per thousand).

Heart failure and *bacterial endocarditis* are the two main causes of death in rheumatic heart disease Heart failure is the functional counterpart of the multiform tissue damage inflicted by the rheumatic state in the individual cardiac components. pericardium, myocardium, endocardium, arterial tree Bacterial endocarditis results from the implantation on the mural and valvular endocardium, chiefly deformed leaflets and cusps, of bacteria accidentally circulating in the blood stream Since rheumatic fever is the main cause of valvular

TABLE 7-6 MISCELLANEOUS MEASUREMENTS IN MITRAL STENOSIS. 50 HEARTS

Measurement	*Range, cm*	*Average, cm*
Intercommissural diameter of valve	0.7 – 2.9	1.9
Anteroposterior diameter of valve	0.1 – 1.5	0.5
Circumference of AV ring	7.0 –14 5	10.4
Thickness left ventricle	1.0 – 2.3	1.4
Depth left ventricle	6.0 –10.5	7.7
Thickness left atrium	0.09– 0.4	0.24

SOURCE From Rusted et al Circulation. 1956.

ponents. One view favors the belief that progressive cicatricial contraction represents the *end result of the primary injury and of the subsequent recurrences.* According to the other view, the valve becomes thicker as a result of repeated deposition on the surface of the cusps, chordae, and commissures of layers of fibrin which becomes converted into fibrous tissue.

Magarey has shown that fibrin deposits on the mitral valves can be found in 7 per cent of nonrheumatic hearts and in 70 per cent of rheumatic hearts. It is probable that the deformity associated with the healing of the valvulitis encourages fibrin deposition. Since this is followed by organization, and this sequence of events may repeat itself many times, the slow development of the stenosis over a number of years can find a satisfactory explanation in this pathogenic mechanism If this concept is correct, it is not unlikely that the injury induced by the surgical relief of the stenosis, either by "digital dilatation" or "splitting," may predispose to fibrin deposition, organization of the exudate, and thus recurrence of the stenosis. An analysis of the results of mitral commissurotomy in 1,000 patients by Bailey et al. (1952b) indicates that stenosis recurred in about 2 per cent of the cases. This condition can be accounted for by the fact that the parts that had been separated surgically became fused again, there was inadequate separation of the leaflets at operation, and active rheumatic endocarditis was present

The ideal response to mitral commissurotomy includes a normal blood flow into the left ventricle. In the presence of aortic valve defects, the correction of the mitral stenosis, and the ensuing improved rate of flow through the expanded mitral valve opening may initiate dynamic abnormalities similar to those arising from progressive pathologic abnormality of the aortic valve (Uricchio and Likoff).

The increased effort required to force the blood through the narrowed mitral opening combined with the effect of some degree of mitral insufficiency account for the *hypertrophy and dilatation of the left atrium.* Back pressure in the pulmonary veins and capillaries will eventually produce *passive congestion of the lungs* The engorged blood channels may rupture, giving rise to *hemop-*

TABLE 7-7 MEASUREMENTS OF CHORDAE TENDINEAE IN MITRAL STENOSIS. 50 HEARTS

Measurement	*Length, cm*		*Thickness, cm*	
	Range	*Average*	*Range*	*Average*
Anterolateral muscle to commissure	0.0–1.9	0 8	0 04–0.6	0.13
Posteromedial muscle to commissure	0 0–2.2	0 9	0 04–0.6	0.14
Anterolateral muscle to anterior cusp	0 3–2 6	1 5	0.04–0.4	0.14
Posteromedial muscle to anterior cusp	0.0–2.7	1 6	0.05–0.5	0.14

SOURCE: From Rusted et al. Circulation 1956.

change of rheumatic fever from that of rheumatoid arthritis. The latter consists mainly of

cytes. Although these focal aggregations of lymphoid cells merely represent a nonspecific pattern of inflammatory reaction, their presence is so characteristic as to be recognized as the most important diagnostic feature.

As for the *subcutaneous nodules*, both in rheumatic fever and in rheumatoid arthritis, they occur in the same locations, namely, in the dermis, fascia, and the tendinous expansion of muscles, and in both conditions the whole nodule is enclosed in an ill-defined fibrous capsule. Compared with the nodule of rheumatoid arthritis, the nodule of rheumatic fever tends to be smaller, is more vascularized, richer in cells, less necrotic, and shows more pronounced granulocytic cell infiltration, including eosinophils (Bennett et al.). *However, in contrast with the slow progress of the subcutaneous nodule of rheumatoid arthritis, which may persist for years, the nodule of rheumatic fever undergoes a gradual organization within a few weeks or months and finally is replaced by fibrous connective tissue.*

The structure of the rheumatic and of the rheumatoid nodules *is almost identical*. In both conditions, it consists of masses of poorly differentiated mesenchymal cells and of foci of fibrinoid necrosis. The latter are fairly regularly encircled by a palisade of radially arranged fibroblasts and connective tissue fibers, which slowly infiltrate and replace the necrotic areas. The majority of investigators believe that fibrinoid alteration of the preexisting fibrous connective tissue is the primary manifestation of the lesion and that the mesenchymal reaction represents a *subsequent* tissue response. However, Collins advocates a reverse sequence of events, namely, that the earliest lesion is the mesenchymal tissue proliferation and that fibrinoid degeneration takes place in the newly formed connective tissue, commencing in the center and *spreading outward*.

That cardiac disorders may arise in the course of rheumatoid arthritis has long been known. There is no agreement, however, on the nature of *the disorder and on the incidence* with which it occurs. According to some investigators, cardiac complications in rheumatoid arthritis are not common; according to some others (Kahlmeter; Young and Schwedel, Bayles), they are rather frequent. A series of clinical and pathologic reports have contributed an impressive accumulation of data in support of the contention that the *heart is frequently involved in rheumatoid arthritis*.

In turn, *Baggenstoss and his group* have presented convincing evidence that the cardiac *lesions of rheumatoid arthritis are practically* indistinguishable from those of rheumatic carditis and that the differences that may be encountered are *rather* quantitative than qualitative. This may be interpreted as indicating one of four main *possibilities*: (1) that rheumatoid arthritis is accompanied by characteristic cardiac lesions which, in their anatomic *manifestations, simulate* those of rheumatic carditis; (2) that rheumatic carditis frequently develops in patients with rheumatoid arthritis; (3) that the cardiac lesions of the patient with rheumatoid arthritis are coincident but not related either to *rheumatoid arthritis* or to rheumatic fever; or (4) that rheumatic fever and rheumatoid arthritis reflect a basically identical *disorder*, with different clinical manifestations. On morphologic grounds, the evidence in favor of the last contention is suggestive; however, it is safer to delay final conclusion until such time as the cause or causes of the two conditions are fully explained.

aortic insufficiency, the opening of the pockets is directed toward the aortic valve; in the *systolic pockets* of aortic stenosis, the opening of the pockets is directed toward the apex of the heart. As Saphir says, "There are in the field of pathology only a few anatomic structures which are so characteristic as to indicate a definite functional disturbance."

DEFORMITIES OF THE TRICUSPID VALVE. Although alterations of microscopic dimensions can be found as frequently in the tricuspid valves as in the mitral and the aortic valves, grossly visible deformities of the tricuspid valve are rarely seen. In the Cooke and White series of 217 rheumatic hearts, only 30 showed tricuspid stenosis severe enough to be considered of clinical significance. Among the 351 hearts with valvular deformities analyzed by Clawson, the tricuspid valve was involved in 42, but always in association with other valvular lesions He was unable to detect a single instance in which the tricuspid alone was affected.

Stenosis and insufficiency are almost invariably associated, but one or the other may predominate. Even in the absence of curling and retraction of the cusps, insufficiency is not uncommon, and this is probably related to right ventricular dilatation and congestive heart failure. Since deformity of the tricuspid valve is almost invariably associated with deformities of other valves, its effects on the heart chambers vary according to the extent and degree of the combined valvular involvement. Well-marked, uncomplicated tricuspid insufficiency is expected to produce *hypertrophy and dilatation of both right chambers*, stenosis, *enlargement of the right atrium* White has indicated that the stenosis must reach a considerable degree (8 cm circumference or less) before it becomes of clinical importance

DEFORMITIES OF THE PULMONIC VALVE While rheumatic fever may affect the pulmonic valve, it rarely leads to deformity, and stenosis and insufficiency are so uncommon that they need not be considered (McGuire and McNamara). Only 2 of the 351 hearts with valvular deformities in Clawson's series showed involvement of the pulmonic valve *Right ventricular hypertrophy* first, then dilatation, as congestive failure develops, are the main effects on the heart chambers

THE VASCULAR COMPONENT OF RHEUMATIC HEART DISEASE

Shortly before the Aschoff nodule came to be regarded as the stigma of the rheumatic state, observations by Rabé brought out evidence indicating that the vascular system, including the coronary arteries, does not escape rheumatic injury. He noted medial degeneration and liquefaction, intimal thickening and fibrosis, and he interpreted these changes as due to a proliferative type of endoarteritis. Takayasu and Geipel confirmed these findings but regarded the intimal proliferation as resulting from the organization of emboli or from an irritative intimal response to implanted emboli Although these interpretations are not consistent with the knowledge that embolic phenomena are infrequent in rheumatic fever, their descriptions of endothelial and collagenous hyperplasia in the intima, fibrinoid deposits in the subintimal connective tissue, and narrowing of lumens and destruction of elastica interna well harmonize with the observations of subsequent investigators.

In keeping with the general characteristics of the tissue response to the rheumatic injury, the degenerative changes in the arterial wall are accompanied by a nonspecific inflammatory exudative reaction and by the appearance of the specific nodule of the rheumatic state. The latter frequently extends from the adventitia into the vessel wall, encroaching upon the lumen and destroying in its path the elastic structures

Although it is proved that the coronary arteries are affected in rheumatic fever, opinions differ as to the frequency with which changes occur According to MacCallum (1924), they are uncommon, Klotz, on the contrary, believes that the finer ramifications are invariably affected, a view shared by Perry. According to Karsner and Bayless, rheumatic fever regularly produces *changes in the coronary arteries*, which basically do not differ from those occurring in the endocardium and pericardium The crux of the matter is whether or not the coronary lesions play a substantial part in contributing to the myocardial damage This problem has been the subject of extensive speculation. The consensus favors the concept that *rheumatic coronary disease definitely interferes with the nutrition of the myocardium*

ETIOLOGY

The correlation between rheumatic fever and *hemolytic streptococci of Lancefield* group A is doubted by few physicians interested in this disease. Acute episodes of rheumatic activity occur as nonsuppurative poststreptococcal sequelae of tonsillopharyngitis The exact etiologic relationship between this organism and rheumatic fever has not been clearly delineated. The role of the agent in this host-parasite relationship depends on unknown or poorly understood factors, while individual host response to the hemolytic streptococci of group A is a likely determining feature in the development of the disease (McCarty, 1956). There is a wealth of circumstantial evidence which supports this relationship to the extent that now compels acceptance.

The frequency with which attacks of acute rheumatic fever follow streptococcal infections varies, but an over-all occurrence of 3 per cent is generally accepted. Subsequent episodes of rheumatic fever are in most instances preceded by a new streptococcal infection, and the rate of attack in a rheumatic individual increases to 50 per cent as compared to the above-mentioned 3 per cent in the general population. Recurrences of the disease can be prevented by carrying out proper prophylactic programs utilizing chemotherapeutic or antibiotic agents, as demonstrated in numerous studies. The increased susceptibility to the hemolytic streptococcus by an individual who has had rheumatic fever is documented, as is the increased frequency with which these patients develop rheumatic fever when compared to persons not having had a previous episode of the disease The prevention of rheumatic recurrences is closely correlated with the reduction of hemolytic streptococci in the throat. Also, rheumatic recurrences have not been observed to follow the other illnesses of childhood which are not caused by the hemolytic streptococcus.

Rheumatic fever follows in the wake of streptococcal infection A high incidence of scarlet fever usually is accompanied by a high incidence of rheumatic fever. A large number of young adults living under crowded conditions is a potential environment for the spread of streptococcal disease. This, in turn, is followed by a high over-all rate of rheumatic fever because of the increased opportunity for complications that follow streptococcal infections Finally, appropriate treatment early in the course of streptococcal tonsillopharyngitis markedly reduces the frequency with which rheumatic fever follows the infection.

Although most investigators accept a relationship between group A streptococci and rheumatic fever, there is some doubt as to whether the organism is the sole factor in the rheumatic state. No quantitative correlation exists between the severity of the initial clinical manifestation of pharyngitis and the development of rheumatic fever. About half of the adults with rheumatic heart disease cannot give a clear history of a streptococcal infection followed by rheumatic fever. Not infrequently an individual presenting an acute episode of rheumatic fever denies having had a sore throat with fever and may reveal only symptoms indicative of a nonspecific upper respiratory infection upon questioning. When an individual has a pharyngitis, usually no manifestations are observed which enable one to predict the complication of rheumatic fever. Why some epidemics of streptococcal respiratory disease are followed by a low incidence of rheumatic fever, whereas following others it is high, is not clear. Infections caused by a few types of group A streptococci have been more notoriously followed by rheumatic fever than others; however, the type specificity does not seem to indicate a "rheumatogenic" factor. The streptococcal infections which are followed by rheumatic fever are usually in the respiratory tract.

Hemolytic streptococci have been demonstrated in the hearts of individuals coming to autopsy during an acute episode of rheumatic fever and were observed to be of the same type as those isolated from the respiratory tract, but on the whole, this finding has been infrequent and inconsistent. The treatment of acute rheumatic fever with penicillin or other antibiotic agents eradicates the organism from the throat but seems to have little effect upon arresting the progressive cardiac process.

EPIDEMIOLOGY

Rheumatic fever seems to progress through four phases, as pointed out by Coburn (1931). The first phase is the initial streptococcal infection which, as mentioned above, may not be clinically manifest. The second phase is

deformity, it may be assumed that the rheumatic state is the factor that most frequently predisposes to bacterial implantation.

The term "bacterial endocarditis" is here used in a broad sense to indicate the formation of thrombotic vegetations, containing bacteria, in the mural or valvular endocardium, without consideration of the clinical designations, "acute and subacute (or lenta)," which, in the light of expert opinion, are matched with difficulty on an anatomic basis.

Of the 1,000 rheumatic patients followed by Jones and Bland, 16, or 8 per cent, died of bacterial endocarditis. Similarly, among the 226 cases of fatal rheumatic carditis analyzed by Wilson, May, and Lubschez, 10 per cent died of bacterial endocarditis. The relationship between the rheumatic state and the superimposed septic endocarditis becomes even more impressive in the light of MacIlwaine's analysis of 296 cases (from eight different series) classified as *endocarditis lenta,* which revealed Aschoff bodies (the selected criterion for rheumatic heart disease) in nearly 45 per cent of the cases.

Two main pathogenic mechanisms have been suggested to explain the high frequency with which microorganisms become implanted on the deformed cardiac valves. According to one mechanism, the bacteria reach the valve *through the blood channels within the valve.* According to the other mechanism, bacteria floating in the blood stream *precipitate and grow* on the valve surfaces. The pertinent question concerning the first mechanism is whether or not the cardiac valves are provided with blood channels. Gross (1921) has shown that fetal valves possess vessels, but that they undergo regression some time before birth and that they persist, in rudimentary fashion, only in a small percentage of persons.

Observations by other investigators (Wearn et al.; Wearn and Moritz) give support to the contention of Gross and make unlikely the possibility of bacterial invasion of normal valves by way of the blood channels. However, since *new formation of blood channels* takes place during the stage of repair and fibroblastic proliferation that follows the acute phases of the rheumatic valvulitis, it cannot be ruled out that, under these conditions, septic emboli can gain access to the already altered valve through intravalvular blood channels.

The role of *trauma* and *stress* have been advocated in support of the other pathogenic mechanism. According to Allen, an important factor in determining the localizations of the bacteria on the valve surfaces is the preexisting valvular fibroblastic deformity which creates a barrier, against which the blood strikes, the resulting impact favoring the implantation of bacteria. He further explains the tendency of the bacteria to localize on the outflow surfaces of the valves because of the fact that they come in contact with a much greater volume of blood than they do on the inflow surfaces. In view of the close relationship between preceding rheumatic valvulitis and superimposed bacterial endocarditis, it is not surprising that the valves most frequently involved in the rheumatic state are the same ones which most frequently undergo bacterial invasion.

RELATIONSHIP BETWEEN RHEUMATIC AND RHEUMATOID HEART DISEASE

Lesions similar to those occurring in the rheumatic heart have been reported to be present in the heart of patients with rheumatoid arthritis.

It is generally admitted that rheumatic fever and rheumatoid arthritis have something in common. In both conditions the basic disorder is a systemic alteration of the collagenous tissue, and in both the heart, joints, and subcutaneous tissue are particularly affected. However, the nature of the relationship is not clear. Clinical experience indicates that not infrequently, and predominantly in the adult, the joint disease of the rheumatic state fails to resolve and slowly progresses into a *chronic polyarthritis* which is indistinguishable from that of rheumatoid arthritis. Few studies have hitherto been reported on the alterations that the synovial tissues undergo in rheumatic fever. According to available information (Collins), an intense, nonspecific, acute inflammation precedes the development of submiliary granulomas. The latter resemble more closely the focal lesions in the subcutaneous tissue than those in the myocardium (Aschoff nodules). In general, the diffuse inflammatory lesion resolves quickly and the granulomas undergo collagenization. Proliferative changes are practically absent, and this, according to Collins, is what differentiates the synovial

economic groups This is probably due to crowded living conditions and inadequate medical care Increased incidence of the disease has been observed in the Armed Forces basic training programs when young susceptible individuals from various communities are crowded together in barracks. This situation also appears to be closely related to environmental conditions which enhance the propagation of streptococcal pharyngitis.

STREPTOCOCCAL INFECTIONS AND THEIR THERAPY

Streptococcal tonsillopharyngitis frequently becomes manifest with the sudden onset of sore throat, pain on swallowing, fever of 102 to 104°F, and observable marked injection of the oropharynx and uvula, with swelling, usually with exudate on the tonsils if they still are present Submandibular cervical adenitis, headache, and abdominal pain, with or without vomiting, may also be present. The history of recent exposure to streptococcal infection, e g , scarlet fever, in the home or classroom is occasionally obtained and reinforces the clinical impression *Unfortunately, many streptococcal infections masquerade as nonspecific acute respiratory disease and go untreated, only to be followed by rheumatic fever* Twenty per cent of streptococcal infections are asymptomatic, and evidence of their having occurred is obtained indirectly, by rises in antibody titer, usually antistreptolysin O Treatment of the preceding streptococcal infection usually prevents the initial attack of rheumatic fever However, such an approach toward prevention of rheumatic fever poses an apparently insurmountable task and is impractical in the overall population unless some means of determining susceptible individuals is developed

Treatment of streptococcal tonsillopharyngitis should be instituted within 2 to 3 days of the onset of the disease, since the longer the delay in treatment, the greater is the possibility of the development of rheumatic fever The type of antibiotic and the dosage used is not so important as the duration of therapy, a course of 10 days is imperative if the organism is to be eradicated and relapses are to be avoided (Rammelkamp et al , 1957) All patients with acute rheumatic fever should be considered as having a streptococcal infection and be treated for such unless an adequate course has been completed.

The bactericidal activity of penicillin for group A streptococci makes this the antibiotic of choice [illegible] streptococci of group A are [illegible] [illegible] cillin G in oil containing 2 per [illegible] [illegible] at 3-day intervals usually eradi- [illegible] for 10 days probably is equally effective. [illegible] of drug consumption must be assured if this route of administration is to be used. A single injection of 600,000 units of *benzathine penicillin G* gives a measurable concentration of penicillin in the serum for 10 days to 2 weeks and is a satisfactory method of treatment in children Chamovitz has recommended identical therapy in adults; but recently one intramuscular injection of 900,000 or 1,200,000 units of *benzathine penicillin G* has been advised. For most streptococcal infections this is sufficient, but probably should be augmented with procaine penicillin in severe infections and those with associated cervical adenitis *Chlortetracycline* and *oxytetracycline* are bacteriostatic antibiotics and less effective in eradication of the organism and the prevention of the sequela, rheumatic fever. Their use, as well as that of *erythromycin*, is reserved for individuals who are allergic to penicillin, therapy again should cover a 10-day period. *Sulfonamide derivatives* are no longer advised in the therapy of acute infections due to hemolytic streptococci.

The early and adequate treatment of group A streptococcal infections has and will continue to lower the incidence of acute rheumatic fever. Nonspecific upper respiratory diseases and those not suspected of being streptococcal in etiology probably do not warrant the indiscriminant use of penicillin in their therapy

DIAGNOSIS

Few diseases in medicine have challenged responsible physicians more than rheumatic fever Even today, with multiple laboratory tests, no single diagnostic procedure is yet pathognomonic for this disease Although rheumatic fever frequently proceeds through the four phases, as outlined above, the clinical manifestations of the acute episode may vary considerably. Only *a low-grade fever* may be present with minimal clinical evidence of car-

Clinical aspects of rheumatic fever

ANTONI M. DIEHL AND TOM R. HAMILTON

Rheumatic fever is a disease which affects all parts of the body and has a special predilection for involvement of mesenchymal tissue. The onset may occur at any time, but children over the age of 5 and young adults seem to be most often affected. The course is unpredictable in an individual case, the prognosis is dependent primarily upon the degree of residual heart damage after an acute episode and upon the prevention of subsequent recurrences of the disease.

May Wilson cites several instances of historic interest of illnesses which in retrospect may be considered rheumatic fever in view of cardiac damage associated with joint involvement. Throughout the late 1800s, much was written about the clinical manifestations of rheumatic fever. The severity of this disease seems to have decreased since 1900. The fall in mortality rates was documented prior to the advent of antimicrobial agents. In spite of this favorable aspect, rheumatic fever continues to be a serious problem of childhood, causing more deaths and long-term crippling in adolescence than any other disease except tuberculosis. The development of prophylactic programs has diminished rheumatic recrudescences, however, the disease still falls in the wake of streptococcal infections, causing many deaths or such extensive damage to the valves that surgical intervention may be indicated and, in some instances, mandatory. Rheumatic fever and its cardiac complication, rheumatic heart disease, will continue as long as there are infections caused by hemolytic streptococci of Lancefield group A, or until fundamental biochemical changes are understood and appropriately interpreted in order to determine why certain individuals are susceptible and how they develop the disease.

Literally hundreds of investigators throughout the world have been working on the problem of rheumatic fever. The names of T. Duckett Jones, May Wilson, Rachel Ash, Ann Kuttner, R. T. Grant, Benedict Massell, and Edward Bland have long been connected with rheumatic fever, particularly in regard to long-term follow-up studies of patients with residual heart damage.

The studies by Bland and Jones seem to depict the *natural course of rheumatic patients* quite well. These authors followed 1,000 patients for 20 to 30 years, completing the reported observations in 1951. Rheumatic heart disease was observed in about two-thirds of the patients when the study was initiated. The average age of the onset of rheumatic fever was 8 years. At the end of 10 years, one-fifth of the 1,000 patients were dead, almost all having been members of the rheumatic heart disease group. This mortality rose to 40 per cent of the original rheumatic heart disease group at the completion of 20 years of observation. Of those without clinically detectable heart disease at the onset, only 11 per cent died in the 20-year period. Most of the patients in the rheumatic heart disease group died of congestive heart failure or superimposed bacterial endocarditis. Of those in whom a greatly enlarged heart or congestive failure was a manifestation at the onset, 80 per cent had died by the end of the 20-year period. Rheumatic pericarditis is an ominous sign as well, 63 per cent of patients thus affected having succumbed by the end of the 20 years. How present prophylactic programs or the utilization of steroids in the treatment of acute rheumatic fever will alter the picture, time and careful analysis will tell.

nitched "seagull" quality apical or midprecor-

ever, may not be due to rheumatic fever. Con-
ical evidence of *cardiomegaly*, particularly if it is progressive and associated with fever, tachycardia, or a triple rhythm, frequently indicates severe activity of the disease. The onset of signs of *cardiac decompensation* in a young individual with a previously normal heart suggests active myocarditis. Shortness of breath and precordial chest pain may predominate among the complaints. Pallor, anemia, and fatigability develop in associa-

ure is absent Leucocytosis may be marked.

The roentgenogram may reveal generalized or specific *enlargement of the cardiac chambers*, possibly with pulmonary edema. Fluoroscopic examination of the heart may be normal, or it may show decreased amplitude of cardiac contractions caused by poor contractility and dilatation of the cardiac chambers

Rheumatic *pneumonitis* may be observed, although it is relatively infrequent. Minimal left atrial enlargement may be the first detectable roentgenographic finding

Electrocardiographic alterations consistent with carditis are often present. Serial tracings are indicated during the acute phase, with particular reference to *prolongation of the P-R interval*. First-degree heart block is observed in one-half of the patients in whom daily ECGs are studied; however, this is usually not practical or feasible. The age of the patient and the heart rate must be considered before stating that a prolonged P-R interval is present. With serial ECGs, an increase of 0.04 sec in the P-R interval in a patient with a constant or slower heart rate indicates first-degree AV block. This block usually disappears, but its persistence does not necessarily signify continued active carditis. Second-degree heart block with a 2:1 or 3 1 ventricular response is less commonly seen Complete AV dissociation is most unusual and may signify a poor prognosis if it is persistent. Although *prolongation of the Q-T interval* is sometimes encountered, the measurement is less reliable and has little advantage over the P-R interval. Changes due to epicardial injury are usually present with pericarditis. *Primary T-wave inversion* of myocardial ischemia is occasionally observed with severe rheumatic carditis.

Chorea. Sydenham's chorea, or chorea minor, may sometimes be a manifestation of rheumatic fever and is characterized by the triad of purposeless movements, muscular incoordination, and paresis, plus emotional instability. Chorea per se appears to be self-limited and without residual. The age distribution and seasonal incidence of chorea are similar to those of rheumatic fever, although uncommon after adolescence and rare beyond the age of 21 years Girls are afflicted two or three times as frequently as boys. The exact relation between chorea and rheumatic fever remains somewhat of an enigma, except in patients with the classic clinical pictures. Some children with so-called pure chorea never develop rheumatic fever, whereas others do The latter can be prevented by prophylactic programs directed toward the hemolytic streptococcus, whereas recurrent episodes of Sydenham's chorea are considered generally to be unaltered by such measures. Nearly half of all rheumatic patients have a history of chorea or will develop evidence of it at some time. Similarly, about 50 per cent of patients with chorea have had rheumatic fever or will present manifestations of active episodes subsequently. Recurrences of chorea are not uncommon. Even with repeated bouts, the child and his parents may be given assurance that adulthood will be free of this embarrassing and incapacitating condition.

The pathologic findings in chorea are inconclusive. Few patients succumb to the disease; normal microscopic anatomy has been described, as well as mild diffuse central nervous system monocytic perivascular cuffing. Severe dehydration may occur as a result of the excessive fluid loss through the skin and lungs or may follow diminished intake due to dysphagia. Dysarthria and difficulty in deglutition are commonly observed. Because of the purposeless movements and muscular paresis, self-inflicted injury must be avoided. Laboratory studies in the "pure" form of chorea are usually normal. The sedimentation rate often is only slightly elevated, an increase should suggest an associated infectious process or rheumatic fever. C-reactive protein is usually normal or negative, as is the antistreptolysin O titer, unless active rheumatic disease coexists.

the so-called *latent period* which usually lasts 1 to 3 weeks, during which the fever and apparently the infection have subsided but the individual does not seem to quite return to normal. This is followed by phase three, which is the *acute rheumatic episode.* The spectrum of manifestations in the patient at this time is broad; on the one hand he may seem only mildly ill, with slight but definite clinical evidence of carditis; on the other hand he may be desperately ill, presenting polyarthritis and progressive carditis with decompensation leading to death. The acute episode lasts a variable length of time, usually 2 to 3 months; occasionally, however, smouldering rheumatic activity may exist for several years. Fortunately, this is the exception. The final period is that of the *quiescent or inactive phase,* during which all signs of rheumatic activity have subsided; the patient may require several weeks or months before he attains the maximum activity that is safely permissible, depending on the residual cardiac damage. If there is no residual rheumatic heart disease, full activity may be resumed This inactive phase lasts for the remainder of the life of the patient unless recurrence of the rheumatic process occurs; this usually follows another infection by hemolytic streptococci. During this phase, prophylaxis against hemolytic streptococci and the infections caused by various types of group A organisms is of utmost importance if recurrences of rheumatic fever are to be prevented

Although streptococcal antibody response in the individual with rheumatic fever (in the form of *antistreptolysin O, antistreptokinase,* and *antihyaluronidase*) can be demonstrated in the majority of cases, most investigators feel that the changes which take place in the development of the rheumatic state are *not* a typical form of antigen-antibody reaction, but rather a *variant of a hypersensitivity phenomenon* (Aikawa). The group A hemolytic streptococci may be the most important or the only infectious agent in the rheumatic state, however, the exact mechanism in the pathogenesis of this disease still remains obscure

Certain *predisposing factors* exist which tend to increase the frequency with which attacks of rheumatic fever follow streptococcal infections. It has been recognized for many years that the siblings of rheumatic children are more prone to develop the disease than children without a sibling history of rheumatic fever. Reporting on studies of rheumatic families, May Wilson pointed out that individuals with histories of close relatives affected by rheumatic fever have an increased predilection to the disease. This may be said also for the offspring of rheumatic parents. In 63 families involving 126 brothers and sisters of rheumatic children followed over a period of 4 years, three initial attacks of rheumatic fever were observed in the previously unaffected siblings. The explanation of this familial characteristic does not seem to rely solely on an increased incidence of streptococcal disease in members of these families, although the epidemiologic aspect is an important consideration. It cannot account for a reported increase in incidence of 14 of 15 affected children in families in whom both parents were rheumatic, of 1 in 4 children affected in families with less strong parental traits of susceptibility.

Several reports have suggested variations in incidence of the disease with *color* and *race* Such differences seem to be more apparent than real and may be explained on an environmental basis which is more favorable to the spread of streptococcal disease Both *sexes* appear to be equally affected, with the exception of the manifestation of Sydenham's chorea; here females are afflicted three times as frequently as males Individuals of all *age* groups are capable of developing rheumatic fever, however, the disease is quite unusual under the age of 4 years and is rare in infancy. The incidence in the later decades of life is low Children between the ages of 5 and 15 appear to have a predilection for rheumatic fever, and the peak incidence for the initial attack is between 6 and 8 years.

Rheumatic fever occurs in *all* climates and geographic locations Cold and damp weather predispose to the disease, and the incidence is greatest in the temperate zones of the United States In North America, attacks of rheumatic fever tend to be at an increased rate in the winter and spring months, with the ebb occurring in early summer and lasting through late fall Rheumatic fever has been reported more frequently in the lower socio-

that the sedimentation rate is not a specific test for rheumatic fever. High or rapid values are *common in various pathologic states* Although *most* patients show an increased sedimentation rate *during an* attack of acute rheumatic fever, normal values are occasionally observed. Unfortunately, even when the rheumatic process is known to be active, *this laboratory test tends to be normal or subnormal in the presence of heart failure* The exact mechanism which b[illegible] about a rapid fall in the sedimentation [illegible]

[illegible] ease An increase in the erythrocyte sedimen*tation rate of a patient suspected of having* rheumatism may be considered as one of the minor criteria for establishing a diagnosis of acute rheumatic fever.

During the early acute phase of rheumatic fever, *C-reactive protein* (C-RP) is observed *consistently Normally, no C-reactive protein is detected in* serum by the conventional method of testing *High values of C-reactive* protein, e g, 3+ or greater, are observed in patients in whom a large *amount* of tissue is involved in the inflammatory process Not infrequently, *C-reactive protein is negative though the patient still has* rheumatic activity, *especially* later in a smouldering form This acute-phase reactant is usually present when the disease process continues unabated or is becoming progressively worse, during rebound activity on premature withdrawal *of therapy,* and in the early *stage of an active* episode Leucocytosis usually *also present, but not* invariably

Prolonged Atrioventricular Conduction. Numerou[illegible] [illegible]ardiographic changes may oc*cur du*[illegible] [illegible]ditis. As [illegible] acteristic, although not pathognomonic, [illegible]tion in the ECG is evidence of delay in the conduction time from the atria to the ventricles. Normal values for AV conduction time vary with age and rate, these are shown in Table 7-8 The P-R interval may be prolonged for various reasons such as a previous attack *of carditis*, digitalization, or a congenital AV block; therefore prolongation does not serve as a specific indication of active rheumatic carditis The diagnosis of active carditis is more *tenable* when the P-R interval becomes progressively longer from tracing to tracing or other types of block develop, such as the Wenkebach periods, second degree AV block (2:1, 3:1, etc.), or complete AV dissociation. In most patients who show a first-degree block during active carditis, the ECG reverts to normal, however, *a small percentage continue* indefinitely to manifest prolonged AV conduction times. The P-R interval, per se, cannot be used as the only criteria for subsiding or quiescent rheumatic activity, except to indicate that the carditis probably *is diminishing as it shortens.* The simple finding of prolonged AV conduction in the ECG is sufficient to permit its use as a so-called minor manifestation of rheumatic fever However, *it is* nonspecific and should not be considered as a *minor criterion* in the *absence* of the major manifestations of carditis. In the experience of Weinstein et al (1955), *studying rheumatic* complications of scarlet fever over a period of 7 years, the majority of

TABLE 7-8 UPPER LIMITS OF THE NORMAL P-R INTERVALS CORRELATION OF AGE AND HEART RATE

	Duration, sec				
	Less than 70	71–90	91–110	111–130	*More than 130*
Large adults	0.21	0.20	0.19	0.18	0.17
Small adults	0.20	0.19	0.18	0.17	0.16
Children, ages 14–17	0.19	0.18	0.17	0.16	0.15
Children, ages 7–13	0.18	0.17	0.16	0.15	0.14
Children, ages 1½–6	0.17	0.165	0.155	0.145	0.135
Children, ages 0–1½	0.16	0.15	0.145	0.135	0.125

SOURCE Adapted from Ashman and Hull *Essentials of Electrocardiography*. Macmillan, 1941.

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complaints in a disturbed family relationship is as important as the overconcerned mother who has been misinformed about rheumatic fever and suspects its existence in her child. Most frequently, the inability properly to fulfill the suggested diagnostic criteria for rheumatic fever leads to further delving into the psychiatric history Steps toward working out these problems should be made while ruling out other organic disease

Rheumatoid arthritis may be difficult to distinguish from rheumatic fever. Subcutaneous nodules may be observed in both diseases Pericarditis and myocarditis occur rarely in rheumatoid arthritis. Usually, no antecedent upper respiratory infection is noted in the latter disease and the antistreptolysin O titer is normal or only coincidentally elevated The joint manifestations of rheumatoid arthritis tend to afflict the smaller joints, such as those of the fingers and hands Several joints may be involved simultaneously rather than in the typical migratory fashion of rheumatic fever In rheumatoid arthritis, permanent joint deformities are observed frequently, both clinically and on roentgenograms. The response to steroids and aspirin is less dramatic, and exacerbation of joint symptoms is common in rheumatoid arthritis when the medications are tapered too rapidly or stopped The acute-phase reactants, such as C-reactive protein, sedimentation rate, and mucoproteins, are abnormal for weeks or months, particularly when antirheumatic drugs are withheld A much longer history of redness and swelling of the joints is noted in rheumatoid arthritis, exacerbations and remissions are commonly the rule The presence of the typical murmur of mitral or aortic regurgitation points strongly to rheumatic fever, as does a previous history of rheumatic fever Exanthemas may be observed in rheumatoid arthritis, but they are commonly of the blotchy, nondescript variety rather than those of the typical erythema marginatum Although Sydenham's chorea occurs rarely in rheumatic fever when active polyarthritis is evident, the coexistence of these manifestations favors the diagnosis of rheumatic fever over rheumatoid arthritis Observation for several weeks or months may be necessary before differentiation is possible On rare occasions, the two diseases have been observed in the same patient.

Other so-called collagen or mesenchymal diseases, such as *lupus erythematosus* and *polyarteritis nodosa*, sometimes must be considered in the differential diagnosis. The presence of the typical butterfly rash on the cheeks and nose favors the diagnosis of lupus erythematosus Lupus erythematosus cells in smears of the peripheral blood are uncommon in rheumatic fever. Much higher values of gamma globulin observed by electrophoresis is characteristic of lupus erythematosus in contrast with rheumatic fever. An atypical history, poor response to therapy, and a prolonged variable clinical course suggest another member of the collagen diseases. Pericarditis or myocarditis may be features of disseminated lupus erythematosus, but definite valvular disease is more common in rheumatic fever.

Poliomyelitis with characteristic muscle spasm and pain, if paresis is absent, may be confused with early rheumatic fever. Antecedent upper respiratory infections are the rule in both diseases Stiff neck, normal white blood cell count, and pleocytosis of the cerebrospinal fluid favor anterior poliomyelitis, whereas involvement of the joints with swelling, redness, or both suggest rheumatic fever, as does evidence of carditis

Abdominal pain may be the earliest symptom of rheumatic fever, but it more likely suggests the existence of a surgical condition. Appendectomies especially may be avoided by noting the atypicality of physical findings on examination of the abdomen. The presence of significant organic murmurs, with or without the joint manifestations, favors the diagnosis of rheumatic fever. The differential diagnosis may be extremely difficult early in the clinical course when pneumonia in the right lower lobe may refer pain to the abdomen

Congenital abnormalities of the heart may produce associated murmurs which can be confused with those of rheumatic heart disease A description of the quality and location of the murmur frequently helps to characterize it and clarify the cause A decrescendo diastolic blow at the left sternal border is most frequently caused by rheumatic aortic regurgitation. Congenital aortic insufficiency without dominant stenosis is rare. The Graham Steell murmur of pulmonary insufficiency secondary to hypertension in the lesser circulation may produce a similar murmur. Evidence of right ventricu-

ditis. *Chorea* or incapacitating *migratory polyarthritis* may coexist with progressive *carditis*. When the latter is present, little question arises as to the diagnosis of rheumatic fever. It becomes more difficult when the rheumatic manifestations are less well delineated and the classic form is lacking. Here is the motivation for intense research to develop, evaluate, and apply laboratory aids in the diagnosis and follow-up studies of rheumatic fever.

T. Duckett Jones (1944) outlined major and minor criteria for the diagnosis of rheumatic fever. These subsequently have been modified by the Rheumatic Fever Committee of the American Heart Association. These symptoms and signs will be subsequently discussed in detail. In the presence of any two major criteria, or one major and two or more minor criteria, a presumptive diagnosis of rheumatic fever can be made. Epistaxis, abdominal pain, various forms of skin rashes, weight loss, anorexia, pallor, and fatigability are observed at times in patients with rheumatic fever. They are nonspecific and common complaints of numerous other diseases, both organic and functional. However, they may serve as leads for further investigation and eventual clarification of diagnostic problems. The final diagnosis must be made only when all factors in the history, physical examination, and laboratory information are considered.

MAJOR MANIFESTATIONS

Arthritis. The first and possibly the most frequent major manifestation is arthritis. This classically involves two or more large joints, either simultaneously or in a migratory fashion, and it is characterized by swelling, local heat, and/or redness, with extreme pain. Because of the discomfort, there is active and passive limitation of motion of the joints. Fever is usually present. Involvement of the joints may vary from day to day, or it may subside completely in one major joint, only to occur in others. It is infrequent to have the arthritis persist for longer than a few weeks, and permanent changes in the joints are not a feature of the periarthritic involvement. The joints of the fingers and toes are sometimes involved, but the knees, ankles, wrists, hips, and elbows are most frequently affected.

The response of these joints to *salicylates* is usually most dramatic (within 24 to 48 hr), and their use has been advocated as a diagnostic aid. Arthritis seems to be less common in younger children than in adolescents and adults. The manifestations of joint involvement may vary in different parts of the country. Little evidence of this part of the clinical picture is noted in California or Florida in contrast to an incidence of about 60 per cent along the Atlantic seaboard in New England.

The association of polyarthritis with fever and an elevated sedimentation rate usually indicates rheumatic fever. However, extreme caution must be taken to exclude other disease states in which this triad of findings is present before concluding that it is on a rheumatic basis.

Carditis. The most important major manifestation of rheumatic fever is the carditis. This may lead to progressive cardiac enlargement and death during the acute phase of the disease. Whereas other manifestations usually leave no serious residual lesions, the cardiac involvement may result in permanent damage to the heart (rheumatic heart disease). The latter is the most feared facet of rheumatic fever since, from its early conduction defect evidenced by prolongation of the P-R interval on the electrocardiogram to the later stages of valvulitis and deformities, it leads to high morbidity and mortality rates. Cardiac involvement in patients with potential or possible rheumatic heart disease may be clinically inapparent at any time during the course of the so-called rheumatic state. Some physicians feel that carditis is almost universally present in association with rheumatic polyarthritis and that cardiac damage may become clinically evident only some years later.

Involvement of the heart presents little difficulty in diagnosis when significant or changing murmurs are present which indicate insufficiency of the aortic or mitral valves. The loud, prolonged *apical decrescendo systolic blow* or the high-pitched *decrescendo diastolic blow* at the left sternal border is rarely overlooked by the clinician. The changing intensity or pitch of these murmurs may be the only sign of the cardiac process being active. A history indicating that there were no heart murmurs until the present illness is sometimes helpful in ruling out quiescent rheumatic heart disease. The development of new significant murmurs is always a sign of *active carditis*. A high-

complaints in a disturbed family relationship is as important as the overconcerned mother who has been misinformed about rheumatic fever and suspects its existence in her child. Most frequently, the inability properly to fulfill the suggested diagnostic criteria for rheumatic fever leads to further delving into the psychiatric history Steps toward working out these problems should be made while ruling out other organic disease

Rheumatoid arthritis may be difficult to distinguish from rheumatic fever Subcutaneous nodules may be observed in both diseases. Pericarditis and myocarditis occur rarely in rheumatoid arthritis Usually, no antecedent upper respiratory infection is noted in the latter disease and the antistreptolysin O titer is normal or only coincidentally elevated. The joint manifestations of rheumatoid arthritis tend to afflict the smaller joints, such as those of the fingers and hands. Several joints may be involved simultaneously rather than in the typical migratory fashion of rheumatic fever. In rheumatoid arthritis, permanent joint deformities are observed frequently, both clinically and on roentgenograms The response to steroids and aspirin is less dramatic, and exacerbation of joint symptoms is common in rheumatoid arthritis when the medications are tapered too rapidly or stopped. The acute-phase reactants, such as C-reactive protein, sedimentation rate, and mucoproteins, are abnormal for weeks or months, particularly when antirheumatic drugs are withheld. A much longer history of redness and swelling of the joints is noted in rheumatoid arthritis; exacerbations and remissions are commonly the rule. The presence of the typical murmur of mitral or aortic regurgitation points strongly to rheumatic fever, as does a previous history of rheumatic fever Exanthemas may be observed in rheumatoid arthritis, but they are commonly of the blotchy, nondescript variety rather than those of the typical erythema marginatum Although Sydenham's chorea occurs rarely in rheumatic fever when active polyarthritis is evident, the coexistence of these manifestations favors the diagnosis of rheumatic fever over rheumatoid arthritis. Observation for several weeks or months may be necessary before differentiation is possible. On rare occasions, the two diseases have been observed in the same patient.

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Alterations in the findings in the spinal fluid are the exception, though mild pleocytosis is occasionally observed.

The clinical course of Sydenham's chorea is variable and unpredictable. Mild attacks may last 6 weeks; however, severe chorea lasts several months. When one attack ends and another begins may not be clear. Emotional lability with periods of crying on slight provocation may persist for a year or more. Polyarthritis is infrequent with chorea, whereas carditis is the most commonly associated major manifestation. Nocturnal remission of choreiform movements is the rule.

Subcutaneous Nodules. The presence of subcutaneous nodules is pathognomonic of rheumatic fever if rheumatoid arthritis can be excluded. These firm, freely movable nodules are nontender, nonerythematous, and usually located over the extensor surfaces of the joints and the occiput They are in the subcutaneous tissue and not attached to the skin or underlying structures, microscopically, there is fibrinoid degeneration, and the appearance is similar to that of the Aschoff bodies observed in myocardial tissue Subcutaneous nodules vary considerably in size from only a few millimeters in diameter to several centimeters, and may attain the size of a small hen's egg. Carditis is not uncommonly associated with subcutaneous nodules, and persistence of the nodules usually indicates continued rheumatic activity From a diagnostic viewpoint, it is unfortunate that rheumatic nodules are not a common manifestation of the rheumatic state. This is not entirely because the search for them is being neglected and they are being overlooked; apparently the frequency with which they occur is diminishing.

Erythema Marginatum. Although numerous types of skin rashes have been described in association with rheumatic fever, including erythema nodosum and multiforme, it is *erythema marginatum* or *annulare* which is the most common It can serve as one of the major diagnostic criteria for rheumatic fever when it is observed in its typical form This particular rash is not pathognomonic of any specific disease, but it is highly suggestive of the rheumatic state (Burke); allergic dermatoses, rheumatoid arthritis, and the skin manifestation of some other generalized systemic disease must also be considered.

Erythema annulare occurs as a red rash anywhere on the body, although it is more commonly found on the trunk, abdomen, and upper extremities. The size of the individual lesions varies from several millimeters to 2 to 3 cm in diameter. The borders are irregular, sharply demarcated, and not elevated. Central clearing of the erythema is common, and the redness readily blanches on pressure No pruritus is associated with it. The lesions may appear and fade within several hours, only to reappear at other sites. Erythema marginatum on a rheumatic basis does not appear during the quiescent phase of the rheumatic process. True erythema marginatum is not observed with great frequency in rheumatic fever. This detracts from its usefulness as a diagnostic feature. However, when it is present, active rheumatic carditis is usually also present or impending, and thus considerable importance may be attached to it.

MINOR MANIFESTATIONS

There are a number of clinical manifestations as well as laboratory findings which are frequently associated with acute rheumatic activity. None of them is pathognomonic, nor must any single one invariably be present for the diagnosis of acute rheumatic fever.

Fever. As the name of this disease implies, fever in the form of a significant elevation in temperature is usually present during the acute phase of rheumatic fever. Although fever may be absent, temperatures ranging from 101 to 103°F are common, especially in patients with migratory polyarthritis. Occasionally the hyperpyrexia is marked However, smouldering carditis may be present when the temperature is normal or only slightly elevated, viz., 100 4 to 100 8°F. The temperature returns to normal or subnormal within a matter of hours or several days after therapy with salicylates or steroids is instituted In untreated rheumatic fever, intermittent fever may be manifest for weeks or months. The unexplained fever and ill health with or without arthritis usually lead the patient to the physician

Sedimentation Rate, C-Reactive Protein, and Leucocytosis. The rapidity with which red blood cells settle or fall in a tube containing a specimen of unclotted blood has been used for years by physicians as a nonspecific indicator of disease activity. It should be emphasized

avoided and very few actual cases missed. The purpose of this section is to point out that rheumatic fever can be easily overdiagnosed and that this can and should be prevented.

Innocent murmurs in the pediatric age group are the rule rather than the exception, occurring in 60 to 70 per cent of normal children if specifically listened for.[1] *Nonorganic systolic murmurs* usually become louder with excitement, tachycardia, and fever The short, rough tambour quality of the functional murmur noted at the left border of the sternum should not be confused with the softer, more prolonged systolic murmur at the apex which occurs with mitral valvulitis or regurgitation. If a murmur does not have the typical quality of acquired rheumatic valvular disease, it should be considered functional or congenital, until proved otherwise.

Arthralgia and myalgia are common complaints of children. When only one joint is involved with pain or swelling, trauma or local infections within the joint should be suspected A generalized *allergic arthritis* may exist if multiple joints are affected suddenly. A history of recent administration of a sensitizing agent augments this impression Unless several joints are involved with pain, redness, or swelling in a migratory fashion, polyarthritis due to rheumatic fever probably does not exist.

Most children are relatively more fidgety and emotionally labile as compared to adults. Unless purposeless movements or muscular paresis is present, Sydenham's chorea probably need not be considered *Habit spasms* and *tics* are differentiated by their repetitive performance involving the same muscle groups Experience has indicated that many so-called "rheumatic suspects" present problems which are basically those of an emotionally disturbed child, they usually stem from anxieties of the parents about rheumatic fever or from the inability of the child to cope with the family or environmental pressures and demands The "poor eater," the "nervous child," the "underweight" boy, and the "easily fatigued" adolescent frequently characterize an emotionally disturbed child as described by the parents. The ever-present cognizance of the possible presence of psychiatric manifestations in children and their parents is rewarding.

Skin rashes in children are common. Erythema marginatum is not pathognomonic for rheumatic fever, although it is highly suggestive of the disease. As mentioned previously, erythema annulare is not commonly seen in rheumatic fever today; when it is present, other major manifestations usually coexist. *Nondescript dermatitides* of a benign nature are frequent and are not a sign of rheumatic fever. Only when the skin rash has the typical appearance of erythema marginatum should rheumatic fever be considered. The blotchy erythematous *toxic rash* occasionally associated with rheumatoid arthritis adds to the confusion in the differentiation between the two diseases.

Fever is a common complaint presented or described by the parents. The term "low-grade fever" is often misleading to the physician and can be misinterpreted. Accurate recording of the temperature should be made when fever is suspected Fluctuations from 97 to 99 6 or 99 8°F is the rule in normal persons Variation of so-called normal temperatures may even register 100 to 100 4°F on a warm day, following exercise, or in the afternoon. Failure by the physician to appreciate *normal variations in temperature* may lead to an erroneous diagnosis of rheumatic fever. Fever is usually present during the acute phase of the rheumatic process, but since it is frequently observed in other diseases, a diagnosis of rheumatic fever is indicated only in the presence of one or more major manifestations.

The *erythrocyte sedimentation rate* is not a specific or diagnostic test for rheumatic fever. It may be elevated in many diseases, infectious and otherwise The sedimentation rate has most value in following the course of the rheumatic disease once the diagnosis has been established No child should be called rheumatic merely on the basis of an elevated sedimentation rate. At times this test may present a high value when no pathologic process of any type can be demonstrated.

C-reactive protein is consistently present in the blood in an early stage of rheumatic fever.

[1] Unexplained, innocent murmurs occur in 60 to 70 per cent of children if one counts grade I murmurs If only murmurs louder than grade I are considered, the percentage drops to 20 to 30 per cent The "innocence" of these murmurs is still one of the points which can be proved only by subsequent developments It is unfortunate that no certain diagnostic criteria have been found, so far In regard to this problem, see Luisada et al, 1958 *Editor,*

the patients with prolonged P-R intervals when they had scarlet fever developed rheumatic heart disease without any classic attack, whereas those without changes in the P-R interval did not develop rheumatic heart disease.

Streptococcal Infection. The historic, clinical, or laboratory evidence of a recent attack by the beta hemolytic streptococcus is sufficient to consider this as a minor manifestation of rheumatic fever. Not infrequently, on careful questioning, one can obtain a history consistent with a streptococcal sore throat having occurred within the past 2 to 3 weeks. The question is, was it adequately treated? The contacts of the child are important regarding the family, close friends, and his classmates. Has there been scarlet fever in the neighborhood or at school, and are other children out of school because of sore throats? It is uncommon for streptococcal disease of the upper respiratory tract to be still clinically manifest at the time of the acute symptoms of rheumatic fever Occasionally, subsiding cervical adenopathy is noted. The throat culture at this time may or may not be positive for hemolytic streptococci

Indirect laboratory evidence of recent streptococcal infection by antibody response in the serum is present in 80 per cent of individuals with rheumatic fever, as demonstrated by a high or rising titer for *antistreptolysin O.* Antistreptolysin O testing has come into general usage It reflects only the antibody response in the serum of individuals who have had relatively recent experience with streptococci which produce antigenic streptolysin O incident to infection *Titers of 333 Todd units or higher may be considered significant* The return of the antistreptolysin O titer to the normal level of the age group has, in the experience of the authors, been about 7 months, however, the titer may remain above this level for 8 months or longer following a streptococcal infection. A significant rise in antistreptolysin O is considered to be three tubes when serial specimens are available The validity of such a rise on serial examinations depends on the fact that it allows for a one-tube laboratory error in opposite directions on two consecutive determinations without misleading one into interpretation as true antibody response evidenced by a significant rise in titer

Other antibodies which respond to streptococci incriminated in rheumatic fever include the streptococcal *antihyaluronidase* and *antistreptokinase* or *antifibrinolysin.* When these two tests are employed, in addition to the antistreptolysin O titer, the patient with active rheumatic fever almost invariably demonstrates an elevated antibody response against at least one of the antigens of the beta hemolytic streptococci, especially of group A Therapy of the streptococcal tonsillopharyngitis may depress the antibody response. Treatment with penicillin in the first 5 days of infection may suppress the antistreptolysin O titer an average of five tubes. However, delay of treatment until the ninth day after the onset of infection resulted in no suppression of the titer of antistreptolysin O.

History of Previous Attacks of Rheumatic Fever or Inactive Rheumatic Heart Disease. Prior episodes of rheumatic fever or Sydenham's chorea are considered of importance in the minor criteria whether residual damage of the heart exists or not. Persons having had one or more previous attacks of rheumatic fever should be suspected of having a recurrence when any of the other major or minor criteria reappear. The stage is set for ready recurrence after a previous attack of rheumatic fever; the incidence of occurrence of rheumatic activity following an infection with group A beta hemolytic streptococci increases from 3 per cent in initial attacks to approximately 50 per cent subsequently.

Polyarthralgia. The complaint of pain in the larger joints is common in rheumatic fever. Often the history of severe arthralgia is obtained with or without clinical evidence of a limp, limitation of joint motion, or accentuation of discomfort upon active or passive motion of the joint. Delineation of the pain in the joint, and not in the muscle or surrounding area, must be made. The presence of aching or pain in several joints may be considered as a minor criteria in the diagnosis of rheumatic fever, provided that migratory polyarthritis is not a major manifestation in the individual clinical picture.

DIFFERENTIAL DIAGNOSIS

Psychiatric disorders and emotional problems are the most common conditions producing confusion in the diagnosis of rheumatic fever. The lack of recognition of nonorganic

ized convalescent center for rheumatic children in a large metropolitan area is questioned only by few clinicians. Such facilities offer advantages in a homelike environment of a hospital. Education of the child is continued, so that he may rejoin his former classmates upon recovery from his illness Social aspects are coordinated with medical supervision during the convalescence and follow-up care The integration of these approaches to the management of the child allows him to have a more satisfactory psychological adjustment to his restricted activity and enables him and his family to have a better understanding of rheumatic fever and its natural complication, rheumatic heart disease, the progress of which now usually can be curtailed or halted.

Graduated Ambulation. Bed rest is recommended until signs of rheumatic activity have abated A program of graduated ambulation is instituted, which covers 4 to 8 weeks During this period, observations are made for evidence of rheumatic reactivation, as well as for tolerance to increased work by the heart. No single sign or symptom signals inactivity of the disease. A favorable observation is the stabilization or regression of cardiac murmurs, the progression of existing murmurs or the development of new murmurs is indication of continued carditis The disappearance of fever and joint pains is a less sensitive sign of quiescence, particularly when patients are on therapy with aspirin or steroids, which suppresses the symptoms rather than corrects the process. Ambulation of patients is probably unwise until anti-inflammatory drugs have been discontinued and the patients are beyond the danger of rebound activity. Useful and encouraging signs are increase in appetite, a progressive gain in weight in the absence of decompensation and edema, and the return to normal of the nocturnal pulse rate. However, these must be evaluated cautiously when steroids or adrenocorticotropic hormones are used C-reactive protein likewise becomes readily negative early in suppressive steroid therapy of attacks of rheumatic fever and is no more a reliable sign of quiescence than is the initial suppression of fever or painful joints The sedimentation rate may remain a useful indicator of activity of the disease once the diagnosis is established. Normal values of the sedimentation rate may be encountered in cardiac decompensation in spite of smouldering activity or in the presence of salicylate or steroid therapy. Suppression of disease activity by corticoids, as noted by the normal sedimentation rate, is not to be misconstrued as rheumatic quiescence. *Serum mucoprotein* and *protein-bound polysaccharide* are least affected by treatment and most closely parallel true disease activity. These laboratory tests have been found helpful in guiding reduction of anti-inflammatory drugs, as well as in instituting ambulation. All factors must be considered in evaluating rheumatic activity. Treatment with salicylates or steroids should be completed before progressing with ambulation. The latter must proceed with further caution when cardiomegaly and residual valvular damage persist.

Anti-inflammatory, Suppressive, and Curative Drugs. Specific treatment of a disease in which the pathogenesis is ill-defined is complex and difficult No medicine is known which is curative for rheumatic fever in that it stops the pathologic process and reinstates normal structure and function.

Aspirin has been used in the treatment of rheumatic fever for many years. Large doses have little advantage over that of 1 to 1½ grains/lb/day (or 120 to 200 mg/kg/day) in divided dosage. Salicylates usually relieve the fever and joint manifestations within a few days. However, controlled studies fail to reveal any reduction in the degree of cardiac involvement during the acute attack when aspirin is used in the treatment. The residual cardiac damage several years later is not reduced in patients treated with salicylates. Aspirin continues to be used in the treatment of rheumatic fever because of the symptomatic improvement and possibly the temporary suppressive effect of the salicylates That salicylates stimulate corticosteroid production and accelerate steroid metabolism has been demonstrated, low levels of serum and urinary 17-hydroxycorticosteroids were observed in rheumatic patients treated with aspirin. However, the mechanism by which salicylates bring about the apparent antirheumatic effect is not correlated with a high steroid level in the serum and urine

Dosages of 45 to 75 grains (3 to 5 Gm) of aspirin per day administered for several weeks have been employed before gradual

lar hypertrophy on the ECG, the accentuated pulmonary 2d sound, and the systolic murmur of the septal defect suggest congenital heart disease. The apical systolic blow of mitral regurgitation is easily differentiated from pulmonary stenosis and septal defects by the location and quality of the murmur. Isolated congenital mitral regurgitation is rare. In the age group of rheumatic patients, the auscultatory findings of an atrioventricularis communis of the septum primum type with an associated cleft in the mitral or tricuspid valve may be similar to those of acquired mitral insufficiency, but the left axis deviation and right ventricular hypertrophy on the ECG clarify the picture when correlated with the indications of increased pulmonary blood flow on fluoroscopic examination.

The history of no murmur having been previously noted suggests an acquired lesion, whereas a murmur dating from birth or early infancy is more indicative of a congenital heart malformation The presence of other major manifestations of rheumatic fever favor this diagnosis Symptoms and signs of cardiomegaly and decompensation are uncommon presenting complaints in an older child with congenital heart disease, but may be the only findings in acute rheumatic fever A relatively high frequency of association of atrial septal defects with rheumatic heart disease was reported by Abbott The clinical recognition of this combination of findings is uncommon, if not rare, in the experience of the authors

Nonspecific pericarditis may be impossible to differentiate from acute rheumatic fever early in the course of the disease Signs of pericarditis, usually with effusion, are present, and changes consistent with epicardial injury are usually demonstrated by the ECG. A large cardiac silhouette is noted on the roentgenogram, and poor pulsations of the heart are observed fluoroscopically Alterations of the white blood cell count, erythrocyte sedimentation rate, and other acute-phase reactants may be observed if this condition is studied in the acute phase An elevated or rising antistreptolysin O titer, and other evidence of previous streptococcal infection suggest a rheumatic nature of the carditis unless streptococcal infection is intercurrent in the nonspecific or benign pericarditis. The absence of polyarthritis and other major manifestations of the rheumatic state favors the diagnosis of acute benign pericarditis, particularly in the absence of murmurs of valvular insufficiency. The clinical course usually clarifies the diagnosis, but occasionally a pericardial tap is helpful, as in purulent effusion.

Acute bacterial endocarditis occurring in a previously normal heart is an uncommon cause of cardiomegaly and decompensation in the rheumatic age group. *Viral myocarditis* and other forms of acute nonspecific myocardial insufficiency must be considered when enlargement is not accompanied by manifestations of the rheumatic state. *Gonococcal arthritis* usually afflicts one joint only and is not encountered in pediatrics. Patients with *sickle cell disease* usually have a normal sedimentation rate, the demonstration of sickle cells in the peripheral blood is helpful. On occasion the two diseases coexist. *Serum sickness reactions* and the phenomena associated with penicillin sensitivity are sometimes difficult to differentiate from rheumatic fever. Frequently the history and clinical course of the patient clarify the diagnosis.

PITFALLS IN THE DIAGNOSIS OF RHEUMATIC FEVER

The mislabeling of a patient as rheumatic is frequently detrimental to the welfare of the individual. The stigmas that are associated with rheumatic fever, the prolonged treatment with the vigorous and continuous prophylactic program which must be followed are not justified if the patient carries this diagnosis although the disease is only suspected and not really established. Rheumatic fever is not a diagnosis of exclusion to be made only by ruling out other disease processes. As long as the heart is normal, it is probably less serious to miss mild rheumatic fever in an occasional patient who has atypical, inconclusive findings than to overdiagnose the disease in persons who actually do not have the malady. Of course, in such a mild reaction, laboratory tests should not lead one astray, especially with experienced consultation. Medicine is not to be practiced in a "cook-book" fashion, and the final diagnosis of rheumatic fever must rely on clinical judgment unless specific laboratory testing compels it By adhering rigidly to the modified diagnostic criteria of Jones, overdiagnosis of rheumatic fever can be

damage in all patients observed with acute rheumatic fever and carditis. However, the earlier therapy is introduced after the correct diagnosis is established, the more likelihood there is of assuring a normal heart in subsequent months or years. Patients who have well-established rheumatic carditis with valvular regurgitation frequently have residual cardiac damage even after being treated with steroids as outlined above. This probably is dependent upon irreversible changes which already have occurred in these instances. In such patients, administration of ACTH or cortisone probably arrests the usual active process.

Side effects of steroid therapy may be considered a calculated risk in a considerable number of patients. The appearance of Cushing-like facies, increase of appetite, acne vulgaris, weight gain, and a general feeling of well being are not indications to discontinue the therapy, as they are temporary and disappear following cessation of the steroid medication. *In the experience of the authors, the judicious use of steroids does not precipitate cardiac decompensation, although digitalization, mercurial diuretics, and a low sodium diet must be utilized when indicated. Routine administration of potassium prevents hypopotassemia during steroid therapy.*

The use of steroids or aspirin is considered helpful in the treatment of rheumatic fever, in addition to bed rest and other supportive measures. Until specific curative antirheumatic agents are available, these and probably other suppressive and anti-inflammatory drugs should be used in the therapy of rheumatic fever. More practical means of preventing initial episodes of rheumatic activity are to be sought in the management of the problem.

Continued Periodic Evaluation. The ambulation program is not necessarily completed at the time of discharge from a convalescent center or upon reaching a state of full activity within the home. Return to regular school may be advised, with additional rest at night and after school in patients with residual cardiac damage.

In general, if the patient is doing well, the initial follow-up examination and evaluation should be carried out after 1 month of this graded activity. The ECG and the laboratory tests (such as the sedimentation rate, cardiac fluoroscopy, or roentgenograms of the heart) are repeated at the time of the first reevaluation. An interval history is obtained, with specific reference to cardiac symptoms, significant respiratory infections, joint manifestations, appetite, and weight gain. If the rheumatic process remains quiescent and the heart is normal, full activity without restrictions is allowed. The amount of permanent residual cardiac damage governs the necessity for restriction of activity. Curtailment of excessive strenuous exercise, competitive sports, and feats of physical endurance is indicated if there is cardiac enlargement or if the ECG demonstrates evidence of ventricular hypertrophy. Adolescent boys with single or double valvular involvement probably should be advised against participating in high-school "varsity" athletics, even though the heart size and ECG are normal. However, utmost care must be taken to avoid overemphasis upon restriction of activity. Encouragement is urged for maximum participation within the suggested limits.

Periodic examination of persons having had rheumatic fever is of extreme importance. When no cardiac damage persists, reappraisal is suggested twice yearly for 5 years and annually thereafter. In the presence of rheumatic valvular disease, examinations are recommended two or three times a year and more often when they are indicated. Regular visits to the physician's office serve several purposes. The doctor follows the rheumatic process, observing the development of cardiac disease in a previously normal heart or for progression of cardiac lesions in a heart which already has been damaged. Changes in restriction of activity are recommended when necessary, and advice is given about cardiac surgery, if the latter is contemplated. Streptococcal infections must be watched, and the patient is instructed to recognize manifestations of streptococcal disease. The doctor-patient relationship is strengthened, and the importance of a continuous prophylactic program against streptococcal disease is reemphasized. *Marriage counseling* is given, with particular reference to hereditary factors and the possible tolerance of the heart to pregnancy when cardiac damage exists. These factors stress medical guidance and supervision of the rheu-

The substance is demonstrable in numerous acute-phase reactions and is not pathognomonic for any disease. It is specific for the early acute phase or an unabated acute reaction. A high or rising titer for *antistreptolysin O* is indicative of antibody response to a relatively recent streptococcal infection; it is not significant in the nonsuppurative complication, rheumatic fever. It is most helpful to obtain observations early enough in order to note the rising titer while following an acute episode of rheumatic activity.

A *history* of a previous attack of rheumatic fever should be challenged from all aspects. A retrospective diagnosis of the disease cannot be made without fulfilling the modified criteria of Jones. Frequently a review of the hospital records or direct information from the physician who originally cared for the patient may clarify a diagnosis, but commonly the picture remains inconclusive. Family history of rheumatic fever should be subjected to similar critical evaluation Complaints of anorexia, lack of weight gain, tiredness on exertion, easy fatigability, low-grade fever, and epistaxis are inconclusive evidence of rheumatic fever This diagnosis may be excluded by the lack of specific major manifestations of the disease. However, these sometimes common and misleading ancillary features in the history may furnish clues to the correct evaluation of the patient in atypical cases presenting difficult diagnostic problems

The rigid adherence to the modified criteria of Jones for diagnosis of rheumatic fever eases the problem considerably for the physician. Apprehension of the child and parent is allayed by excluding rheumatic fever when this diagnosis is only suspected To state that rheumatic fever exists when inconclusive symptoms and signs are present is unwarranted and may lead to a major disservice to the patient and his family.

MANAGEMENT OF THE PATIENT—RATIONALE OF SPECIFIC TREATMENT

Therapeutic measures in rheumatic fever, in which the steps in pathogenesis are not all clear, have been based primarily on theory or circumstantial evidence and past experience rather than on medical facts Only in recent years have investigative and particularly prophylactic studies pointed conclusively toward the etiologic relation of group A beta hemolytic streptococci to rheumatic fever, most recent evidence has indicated the altered pituitary-adrenal function in this disease. Treatment is considered from several aspects in this section. Previously discussed were therapeutic measures to eradicate the initial streptococcal infection. The same course of antibiotic agents should be administered as the first step in the treatment of the acute phase of rheumatic fever if the streptococcal infection has not been already treated adequately The use of 600,000 units of *procaine penicillin G* in 2 per cent aluminum monostearate by injection, every other day for five injections, is probably the surest method of eradicating the organism. It is important to extend adequate penicillin therapy over a period of 10 days. Prophylaxis for subsequent infections is started simultaneously and will be discussed below.

Importance of Rest. Sibson introduced *bed rest* in the treatment of rheumatic fever over 80 years ago on the premise that a diseased organ, such as the heart, should be placed at minimum working capacity. For healing to be optimum, rest and immobilization was a rule and, since the heart cannot be splinted, bed rest was attempted in an effort to reduce the cardiac work. The hypothesis that rest might minimize the degree of cardiac inflammation and, therefore, reduce the amount of residual scarring and damage has been passed down through the years and is practiced today Sibson and later Taussig and Goldenberg presented suggestive, though inconclusive, data that rest lowered the incidence of residual heart damage Controlled studies have not been carried out to answer this question, and possibly justifiably so, because one hesitates to risk additional cardiac damage for a child Until conclusive evidence can be demonstrated to the contrary, bed rest followed by graduated ambulation should be adhered to. Such a program entails several months of close supervision and medical observation.

Prolonged bed rest is frequently difficult to maintain in the environment of the home. This is especially true when large families are living in crowded conditions Numerous factors, such as expense and lack of educational facilities, in most instances make confinement in a general hospital for acute cases impractical. The importance of the role of an *organ-*

served during the first several months after initiation of the chemotherapeutic agent. Scarlatiniform and morbilliform eruptions are indications to discontinue this medication temporarily or to change to a different prophylactic agent. Sometimes readministration of the sulfadiazine is not associated with recurrences of skin rashes, however, urticarial reactions indicate that the drug should be discontinued. Depression of the bone marrow activity apparently is uncommon (the authors have not encountered this reaction). A fall in the total white blood cell count below 4,000 or in the polymorphonuclear leucocytes to less than 35 per cent is an indication to switch prophylactic agents Renal toxicity and sulfonamide crystalluria is not encountered when only prophylactic doses of sulfadiazine are given, unless there is marked oliguria. Because *sulfadiazine is a bacteriostatic agent*, it is not the drug of choice in the treatment of streptococcal infections Of importance and worthy of consideration is the fact that some strains of group A streptococci develop resistance to sulfadiazine The sulfonamides are most useful in streptococcal prophylaxis when sensitivity to penicillin exists and when the above contraindications do not pertain in the individual case

PENICILLIN Since penicillin is the preferred antibiotic agent in the treatment of streptococcal tonsillopharyngitis, it is probably also the most desirable agent in the prophylaxis of rheumatic recurrences Because the question of actual drug consumption is ever-present, the efficacy of *oral penicillin prophylaxis* in a controlled series is difficult to evaluate The effective minimum dosage for oral administration remains undetermined The Committee on Prevention of Rheumatic Fever of the American Heart Association recommends 200,000 to 250,000 units twice daily, preferably ½ hr before meals Although an empty stomach was suggested, it is probably not necessary for adequate drug absorption *Benzathine penicillin G* and *phenoxymethyl penicillin* (*penicillin V*) given orally in comparable dosage may prove equally effective No strains of group A streptococci resistant to penicillin have been reported thus far The relative ease of administering oral penicillin would also justify its use, if one is certain that it is being taken continuously by the patient

Penicillin remains more costly than sulfadiazine in spite of the marked reduction in price during recent years. Like the sulfonamides, penicillin must be maintained throughout the year, the lack of assurance of daily administration is the most frequent cause of breakdown in a prophylactic program. Generalized toxic reactions of the serum sickness type and angioneurotic edema are indications to discontinue penicillin. In the presence of the [illegible] may [illegible] disappear.

OTHER ANTIBIOTIC AGENTS. *Oxytetracycline*, *chlortetracycline*, or *erythromycin* is employed in hypersensitive individuals who are allergic to penicillin and sulfadiazine. Because of the expense and the fact that most of these agents are bacteriostatic, their use is reserved for such unusual situations Minimum effective dosages have not been determined.

The Intramuscular Route of Administration. A long-acting form of penicillin, *benzathine penicillin G*, was introduced by Stollerman in 1952 as a feasible means of preventing rheumatic recurrences. The effectiveness of benzathine penicillin G in a dosage of 1.2 million units given intramuscularly every 28 days as a prophylactic agent for streptococcal infections in rheumatic subjects is documented Our experience with this method of prophylaxis now covers more than 6,000 patient-months without a recurrence of rheumatic fever. Follow-up of the patient is more feasible since he must return at 4-week intervals. Injection is the only method by which the physician is assured that the antibiotic agent is actually entering the body. Suppression of streptococcal disease is more effective, because this dosage not only is effective in eliminating the carrier state, but eradicates the organism in an individual who has an acute streptococcal infection of the upper respiratory tract. Expense to the patient is ultimately less, and the errors incurred with oral medication are eliminated. Urticaria and erythematous rashes usually do not necessitate discontinuance of this form of prophylaxis.

The principal disadvantage of intramuscular benzathine penicillin G is the pain during the injection of the material and that noted up to 48 hr later. No child has been dropped from our prophylactic program or switched

reduction and final discontinuance of the drug. Another method of treatment with aspirin utilizes the drug only during the time of fever and joint manifestations, with frequent trials off medication, to observe whether joint pain and fever recur. Ambulation is probably contraindicated until it can be determined with certainty that the rheumatic process is quiescent after withdrawal of the suppressive influence of salicylates. Conclusive evidence is lacking to justify the statement that aspirin, even in massive doses, affects the outcome of residual heart damage.

The use of *cortisone and adrenocorticotropic hormone* (ACTH) in the treatment of rheumatic fever introduced much controversy in the medical literature. Uncontrolled studies and single case reports added to the dilemma. Steroids unquestionably have improved the patients symptomatically, with reduction of fever and joint manifestations and depression of the erythrocyte sedimentation rate. Could such treatment prevent further cardiac involvement by the rheumatic process and was the amount of residual heart damage substantially reduced by such treatment? These questions were raised and still need answering

A large cooperative project involving 497 children failed to demonstrate any significant difference between treatment with cortisone, ACTH, and aspirin with regard to their suppressive effect upon major manifestations during the acute phase or upon the amount of residual cardiac damage No superiority of steroids over aspirin in the treatment of adults with rheumatic fever was reported in the study of Hauser et al. Factors such as dosage, length of treatment, and the time in the acute phase at which steroids are introduced may influence the course of the disease A favorable outcome was produced after large amounts of hormones (up to 400 mg of cortisone daily) were administered for 1 week, then suddenly stopped, according to the report of Wilson and Lim No difference was noted between the heart murmurs of 50 hospitalized patients treated with hormones and those of 50 patients treated with aspirin. However, the general impression of several workers is that steroids are superior to salicylates in the severe forms with congestive failure Their prompt use may be lifesaving

High values of cortisone in the serum of patients with acute rheumatic fever were demonstrated early in the course of the disease (first week) and subnormal levels thereafter. High values of ACTH were present in the serum of children with rheumatic fever. Significantly, fewer residual murmurs were detected in 46 hormone-treated children than in 31 patients who received aspirin or only bed rest, as reported by Done et al These patients were all observed in their first attack of rheumatic fever and had no clinical evidence of carditis at the time therapy was instituted. Kelley recommended 3 mg/lb/day of *cortisone* in divided doses (6 6 mg/kg), or 1 I.U./lb/day of ACTH with 500 mg of *ascorbic acid*. This medication was continued until there were no longer any clinical signs of rheumatic activity, the sedimentation rate was depressed for 1 week, and the serum mucoprotein (tyrosine) level was less than 6 mg per 100 ml. The dosage of steroids was then reduced by one-half every second to fourth day, after checking the sedimentation rate before each reduction. When the sedimentation rate rose to abnormal values, the hormone was maintained at this dosage for several days and then again tapered when the sedimentation rate returned to normal The total course ranged from 23 to 105 days These patients received a total dosage of 1,480 to 14,623 mg of cortisone and 1,455 to 4,795 I U of ACTH.

Another treatment schedule is 300 mg of cortisone per day (75 mg every 6 hr), regardless of weight and age, until signs of rheumatic activity are no longer present or are suppressed (usually 7 to 10 days). This dosage is then tapered by 25 mg every other day until discontinued The total course covers 6 to 8 weeks, totaling an average of 5,400 mg of cortisone. Rebound with laboratory evidence (elevated sedimentation rate and reappearance of a positive test for C-reactive protein) has been observed in one-fourth of the patients, but it usually has little immediate clinical significance.

Individualization of dosage of steroids to the patient possibly represents a truly logical contribution to the current approach of steroid therapy. This form of treatment is not effective in preventing permanent cardiac

4

Clinical aspects of rheumatic heart disease

DANIEL ROUTIER

MITRAL STENOSIS

The occurrence of "pure mitral stenosis" is rarely observed.[1] It is seldom found in children, either as a congenital or as an acquired lesion. Mitral stenosis is more frequent in females than in males and is usually found after the fifteenth year of age. Routine examination allows an early diagnosis before the appearance of any symptom.

Symptoms. Respiratory disturbances are the first and most important symptom They draw attention to the disease and recur often during its evolution *Exertional dyspnea* often is responsible for the first medical examination. Dyspnea appears early but may not be manifest for many years in spite of an active physical life; it may not be observed until after several pregnancies *Paroxysmal dyspnea* is another possible disturbance.

The history often includes other symptoms such as *cough, expectoration* (which may be foamy, white, pink, or red), and tracheal rales or laryngeal crackling All these signs are important because they are evidence of congestion of the respiratory apparatus

Precordial pain and *palpitation* are frequently mentioned *Pain* is often localized on the left side, in the submammary or subclavicular area It is usually described as "a painful spot" or "a sensation of pricking," less often as "a constriction" at the cardiac apex. Pain often causes a great deal of anxiety to the patient when it radiates to the left arm, evoking the pain of coronary heart disease. This pain appears suddenly and may last for hours or days, but it is never so severe as to cause interruption of physical activities.

Palpitation is common. It appears after an emotion or an effort and lasts for periods proportional to the intensity of the cause. It may be accompanied by arrhythmias or tachycardia.

In young patients, the sinus rhythm is preserved and *tachycardia* is moderate, usually below 120 Attacks of *supraventricular tachycardia* or *paroxysmal atrial fibrillation* can be observed. In older patients, atrial fibrillation is the rule To these initial symptoms should be added the acute attacks of *pulmonary edema* following physical exertion or the *cerebrovascular attack* followed by hemiplegia.

The prime importance of the respiratory phenomena becomes evident after one realizes that mitral stenosis causes an obstacle to pulmonary venous return Pulmonary flow cannot increase when needed, resulting in hypoxie of the tissues. Pulmonary venous congestion is responsible for alveolar transudation and sudden hemorrhages, manifested by laryngeal crackling, *hemoptysis*, or discrete pink expectoration.

Pulmonary hypertension may sometimes play a role in causing palpitations, tachycardia, and arrhythmias.

[1] Data of left heart catheterization indicate that pure mitral stenosis *does* occur and that predominant stenosis is not rare. *Editor*

reduction and final discontinuance of the drug. Another method of treatment with aspirin utilizes the drug only during the time of fever and joint manifestations, with frequent trials off medication, to observe whether joint pain and fever recur. Ambulation is probably contraindicated until it can be determined with certainty that the rheumatic process is quiescent after withdrawal of the suppressive influence of salicylates. Conclusive evidence is lacking to justify the statement that aspirin, even in massive doses, affects the outcome of residual heart damage.

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Individualization of dosage of steroids to the patient possibly represents a truly logical contribution to the current approach of steroid therapy This form of treatment is not effective in preventing permanent cardiac

However, this explanation if not always satisfactory (Routier et al., 1942). *In certain cases, no occlusive embolus can be found in the lumen of the arteries, even if the picture is typical, while the artery is spastic.* Therefore, an *arterial spasm, maintained long enough, may be responsible for the formation of a "clot" below the spastic area.* This explanation is the most likely in cases of transitory cerebral accidents (hemiplegia, aphasia, confused state, epileptic manifestations) that disappear without leaving neurologic alterations On the other hand, it is possible that arterial spasms are initiated by small emboli

The thromboembolic phenomena of the systematic circulation can occur anywhere but are *more frequent in the legs.* A bilateral obstruction occurs if the embolus is arrested by the bifurcation of the aorta (*saddle embolus*). The patient then suffers a *paraplegia* and is unable to walk or even stand up Visceral infarcts. softening of the brain, obstruction of the mesenteric artery are followed by a number of functional and physical signs Renal and splenic infarcts are usually found at autopsy

Pulmonary infarcts are caused by clots coming from the right heart or the periphery or by local thromboses Large or multiple small infarcts may elicit an acute pulmonary hypertension over and above that resulting from mitral stenosis. And so begins the syndrome of *acute cor pulmonale* with vascular collapse, dyspnea, and cyanosis

Physical Signs and Their Diagnosis. Mitral stenosis is characterized by a sequence of acoustic phenomena first described by Duroziez The *1st sound* is snapping, sometimes very loud, preceded by a *presystolic murmur "in crescendo"* At the beginning of diastole, there is a snapping sound (*opening snap of mitral valve*) followed by a diastolic rumble This constitutes the *diastolic rumble with presystolic accentuation* When the diastolic rumble is of sufficient intensity, it *is accompanied by a diastolic thrill* It is necessary to separate the rumble, which is in decrescendo, from the presystolic murmur, which is short, in crescendo, and ends suddenly with the first sound If there is atrial fibrillation, the presystolic murmur disappears while the diastolic rumble is quite evident However, in atrial fibrillation with a rapid ventricular rate, one may have the impression that, in the short diastoles, there is a crescendo murmur; this is due to the tumultuous filling of the left ventricle.

When the diastolic rumble is typical, it cannot be confused with any other type of murmur. Unfortunately sometimes it is less typical. *Exertion* usually modifies the atypical murmur, which then becomes typical. Another maneuver *which should always be tried is* that of placing the patient in the *left lateral decubitus. This brings the apex closer to the* chest wall and allows a more accurate perception of the murmur. In the differential diagnosis, it should be kept in mind that an aortic diastolic murmur immediately follows the 2d sound while, in the case of a *mitral diastolic* murmur, there is a gap between the 2d sound and the beginning of the murmur.

Another important auscultatory sign is *splitting of the 2d sound* The two phases of this are close, so that there is no difficulty in differentiating this phenomenon from the simulated splitting because the 2d sound is followed, after a pause, by the opening snap of the mitral valve

Upon *auscultation*, the distinction between these two phenomenon can be made by observing that the split 2d sound can be observed only in the 2d and 3d left interspace while the opening snap either is present in the 3d or 4th interspace or can be heard over a wide area The intensity of the 2d pulmonic sound is of importance because its increase indicates the existence of an elevated pulmonary arterial pressure Potain, at the end of the last century, described three evolutive phases of mitral stenosis In the first phase, aortic pressure is higher than pulmonic and the 2d sound is louder at the 2d right intercostal space Later, *the pressure becomes equal in both vessels and there is equality of sounds on both sides of the sternum.* Finally, the pulmonary pressure becomes higher than the aortic, *and splitting* appears at the 2d left interspace.

The opening snap of the mitral valve is the *most* characteristic element and often can be *heard all over the precordial area. It is so called because it is* due to a vibration of the hard and sclerotic mitral valve.

A systolic murmur either soft or harsh, may

matic patient as the most important features in a favorable prognosis.

PROGNOSIS AND COMPLICATIONS

The *immediate outlook* for the patient with rheumatic fever is dependent upon the degree of carditis and the point at which activity of the disease ceases. Occasionally, rheumatic carditis progresses relentlessly, terminating in death. *After the acute and convalescent phase subside,* prognosis is determined by the degree of residual heart damage, the ability to prevent rheumatic recurrences, and the complications of the cardiac disease. The inability of the heart to adjust to residual valvular defects leads to cardiac insufficiency and decompensation. *Recurrences* of rheumatic fever usually usher in more progressive cardiac involvement and damage. Surgical intervention undoubtedly prolongs life expectancy in certain serious complications with irreversible valvular damage. Bacterial endocarditis, superimposed on damaged valves, also governs the prognosis, as do such complications as atrial fibrillation and embolization Restriction of physical activities in the presence of cardiac damage probably has a favorable effect on the prognosis.

PREVENTION OF RECURRENCES

Attacks of rheumatic fever are not associated with immunity to subsequent episodes of the disease As a matter of fact, the opposite seems to apply, with recurrences usually occurring in 50 to 70 per cent of the cases These are almost invariably preceded by streptococcal respiratory infections Treatment of streptococcal sore throats reduces the incidence of recurrent rheumatic fever but does not invariably prevent subsequent attacks *All persons who have had one or more attacks of rheumatic fever should be on a continuous prophylactic program to prevent streptococcic infections and thereby eliminate subsequent episodes of the disease* The preference of drugs, their dosage and route of administration may continue to be individualized Sulfonamides, penicillin in various forms, and the so-called "broad-spectrum" antibiotics have been employed with varying degrees of success. Unless there is individual sensitivity, *penicillin is the prophylactic drug of choice,* because of its bactericidal effect on the group A streptococci and the lack of resistance of these organisms to this antibiotic.

Oral Prophylaxis. Ease of administration of oral antibiotic and chemotherapeutic agents renders this route of prophylaxis advantageous in the majority of patients. Most children who have had rheumatic fever are over the age of 5 years and therefore have little difficulty in swallowing tablets; palatable liquid forms are available for those few who have difficulty. The primary disadvantage of the oral route of administration is the ever-present question of whether the child actually takes the medication. The supply of the prophylactic agent may be allowed to become exhausted and not be replaced, even with conscientious parents The child may dispose of the tablet in the wastebasket or toilet because he does not understand the importance of daily drug administration. Treatment of all siblings with the prophylactic agent is occasionally carried out by parents without advice of a physician When administration of an appropriate antimicrobial agent can be assured, recurrences of rheumatic fever are extremely rare When subsequent bouts of the disease do occur, history of a "break" in prophylaxis can almost always be ascertained as the cause. Because return to the physician's office is necessary every 28 days when utilizing intramuscular injections of a long-acting form of penicillin, closer supervision of the rheumatic patient is possible. Whenever streptococcal infection is suspected in a rheumatic subject on oral prophylaxis, therapy should be instituted to eradicate the organism.

SULFONAMIDES. Experience has shown the effectiveness of *sulfadiazine* as a prophylactic agent in preventing recurrences of rheumatic fever This chemotherapeutic agent should be given in a dosage of 1 0 Gm daily for older children and adults, for those weighing under 60 lb, 0 5 Gm possibly suffices The drug should be taken throughout the year Sulfonamides have the advantage of being inexpensive and are effective in reducing recurrences to about 2 per cent *Gantrisin* and other newer sulfonamides are also effective.

Sulfadiazine has several disadvantages, varying in importance, the primary objections are related to comments relative to all oral administrations. Although toxic reactions are infrequent, they do occur; they usually are ob-

However, *this explanation* is not always satisfactory (Routier et al, 1942). In certain cases, *no occlusive* embolus can be found in the lumen of the arteries, even if the picture is typical, while the artery is spastic. Therefore, an *arterial spasm*, maintained long enough, may be responsible for the formation of a "clot" below the spastic area. This explanation is the most likely in cases of transitory cerebral accidents (hemiplegia, aphasia, confused state, epileptic manifestations) that disappear without leaving neurologic alterations. On the other hand, it is possible that arterial spasms are initiated by small emboli

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to oral medication because of the discomfort associated with injections per se. Various substances are being added to the benzathine penicillin G in an effort to reduce this unfavorable complaint, and when appropriate ones are available, the primary objection to this form of prophylaxis will be lessened. The intramuscular use of 1.2 million units of benzathine penicillin G every 4 weeks is the surest prophylactic method to prevent recurrences of rheumatic fever when there is doubt of the cooperation of the patient on oral medication.

Treatment of Chorea. Therapy is primarily supportive or should be directed toward the rheumatic fever if present. Sedation and removal of stressful situations diminish the purposeless movements, whereas excitement augments them. Little alteration in the course of chorea is derived from administration of steroids or adrenocorticotropic hormone. Limitation of activity and bed rest only need to be consistent with the degree of muscular weakness or with the coexistence of rheumatic fever. Prophylaxis against streptococcal infections is indicated in all patients with chorea; it should be continued through adolescence and then stopped only if a normal heart is present and the socioeconomic conditions, and family and other exposures, are not unfavorable to the patient. The exact duration of prophylaxis should then be determined in the individual case

Physical Signs. Is there an auscultatory sign typical of mitral insufficiency? *The author does not believe so.* Our predecessors taught us that the fundamental sign is an *apical systolic murmur*, either loud or moderately loud, occasionally accompanied by a thrill, radiating *to the left* axilla and heard, at times, posteriorly It is evident that such a murmur can hardly be denied as being related to mitral insufficiency, yet it remains to be demonstrated that such a murmur is produced by actual backflow of blood through the valve. Marey said so, but we are not fully convinced[5] In this respect, one should consider also the existence of reflux of blood without murmur; this is particularly encountered in cases of mitral insufficiency and stenosis In pure mitral insufficiency, even though the murmur is frequently present, it is not constant, its intensity varies considerably from case to case without being proportional to the severity of the reflux A thrill is present only with a very loud murmur. The radiation of the murmur to the axilla and posteriorly is mostly related to the volume of the heart, which is more or less in contact with or separated from the thoracic wall One may point out that mitral insufficiency causes left ventricular enlargement, however, this is far from being always true On the other hand, the murmur may be produced by left ventricular enlargement alone or because of a functionally disturbed ventricular contraction Thus, the increased volume of the left ventricle cannot be used to evaluate the degree of damage of the mitral valve In conclusion, the only auscultatory sign is a long apical systolic murmur, with or without thrill, with or without left ventricular enlargement When this is loud, the chances are that mitral insufficiency is present and severe, on the other hand, if the murmur is faint or soft, regurgitation is likely to be less or absent

Evolution. Pure mitral insufficiency, at least in its mild form, does not seem to alter significantly the hemodynamics, thus, no functional signs are present and life expectancy is unaffected This can be true only if the valvular lesion remains strictly localized, with only mild myocardial lesions or none Acute rheumatic fever tends usually to produce mitral stenosis, and the *frequently* associated *mitral insufficiency is hemodynamically insignificant.* However, at times, insufficiency may be greater than the stenosis. Less often the process evolves toward the so-called pure mitral insufficiency, which is nonevolutive and has a not too severe prognosis. The situation is different when mitral insufficiency is associated with severe myocardial lesions, such as that revealed by progressive dilatation of the heart ("myocardie" according to Laubry). Then the prognosis is based on the latter, and the diagnosis of mitral insufficiency should not be based upon the apical systolic murmur only, but should be demonstrated by fluoroscopy or left heart catheterization. A dilatation of the left ventricle does not exclude the coexistence of a tight stenosis of the mitral valve. Moreover, the systolic apical murmur (at times, very loud) which is produced in a dilated left ventricle is not necessarily a sign of mitral insufficiency (so-called "functional insufficiency"). This type of regurgitation may occur, but it is much rarer than the systolic apical murmur, which probably has another mechanism.

[5] Intracardiac phonocardiography in the left heart has proved that this concept is correct (Luisada and Liu, 1958) *Editor.*

AORTIC STENOSIS

Aortic stenosis is often first noticed and diagnosed in a routine examination of infants, adults, or old people This means that this valvular lesion may develop and progress for a long time without causing symptoms. At times, it may be silent for many years until the development of cardiac failure, and the latter is often irreversible and not influenced by treatment. However, there are cases where *symptoms occur*, so that the patient seeks consultation.

Symptoms. In the infant, *congenital aortic stenosis* is generally symptomless It is usually diagnosed early in life by the pediatrician in the course of a routine checkup because of the loudness of the murmur. Sometimes it is first diagnosed following a typical attack of *fainting*, which occurs while the child is in full activity This is a typical *syncope* and cannot be mistaken for epilepsy After a few seconds, the patient regains consciousness and is aware of his surroundings. The physician called after this episode cannot possibly miss the loud aortic systolic murmur, which is characteristic of aortic stenosis, this murmur is

Stenoses of comparable degree are tolerated to different extents by various patients, partly on account of different psychic reaction.

A *stabilized mitral stenosis*, i.e., one which is not complicated by an active rheumatic process, behaves as an inert scar. In such cases, the only effect is on the pulmonary circulation If the mitral narrowing is moderate, cardiac compensation is possible and there may be a satisfactory degree of health for a normal life span. On the other hand, a severe *mitral block* allows only a severely reduced flow and should have a poor prognosis. With a narrow mitral passage, all the circulatory system is affected, even though the pulmonary circulation shows the greatest evidence of the dynamic disturbance. The syndrome includes attacks of *pulmonary edema*, severe pulmonary hypertension, and right ventricular failure with hepatic engorgement and peripheral edema.

Differential diagnosis between a stabilized picture and a form in evolution may be based on the *temperature curve* There may be either a febrile or a subfebrile course, in spite of normal laboratory findings antistreptolysin titer, sedimentation rate, and the fibrinogen test are often normal In such cases, there is no recurrence of rheumatic fever and the main factor is a slow and constant increase of the valvular scar which tends to narrow the opening, to thicken and harden the walls of the valvular funnel and the chordae tendineae, and to facilitate calcification [2] This stage, is called the *stage of evolution* Blood cultures are nevertheless necessary in order to rule out a bacterial endocarditis

During the period of evolution, the temperature is elevated and a variety of accidents may occur. disturbances of rate and rhythm, thromboembolic phenomena, pulmonary manifestations, or episodes of right ventricular failure. It is, therefore, important to take the patient's temperature regularly.

Alterations of Rhythm. During the period of stabilization, episodes of tachycardia may occur. On the other hand, the period of evolution is characterized by the onset of *atrial fibrillation*. The patient may be unaware of the onset of this disturbance, so that he is often unable to tell how long his pulse has been irregular.

This arrhythmia may be the cause of fatigue, epigastric pain, and increase of exertional dyspnea. These symptoms are not directly caused by the arrhythmia, but rather by the process of evolution of the cardiac lesions.

The ECG often shows *ventricular extrasystoles* that have no special prognostic significance, even though they reveal the increased irritability of the myocardium due to the inflammatory process. It is common to observe persistent tachycardia. This may be due to *sinus tachycardia*, *ventricular tachycardia*, or *atrial flutter*. All of them are scarcely modified by digitalization during the inflammatory period. Less common are disturbances of conductivity consisting of *AV block*, *BBB*, or *interventricular block*.

Respiratory Paroxysms. During the period of stabilization, mitral stenosis is often accompanied by a certain degree of evertional dyspnea and by an increase of functional disturbances during the premenstrual period. During the phase of evolution, the respiratory embarrassments usually occur in the form of *acute pulmonary edema* after slight evertion or at night. Prior episodes are revealed by tracheal rales, laryngeal crackling, or cough with slight foamy expectoration. In certain cases, *hemoptyses* are common They are due to the intense congestion of the bronchial tree, with rupture of anastomotic varicose bronchial veins In some cases, blood may come from ruptured pulmonary capillaries. These accidents are apparently due to pulmonary hypertension, but this is not the only factor.

Thromboembolic Phenomena. These accidents, resulting from arterial obstruction, can be followed by ischemia and gangrene of the limbs, of one of the viscera, or of an area of the lungs In certain cases, the embolus seems to come from *phlebothromboses* of the legs or from *mural thrombi* of the right atrium; then, the result is an obstruction of the pulmonary artery or one of its branches. In other cases, there is a *mural thrombus* of the left atrium and an obstruction of one of the peripheral arteries (brain, spleen, legs, kidney, etc.).

[2] This original concept is still far from being accepted. Most authors admit that the evolutionary stage is caused by a silent recurrence of rheumatic carditis. *Editor*

admitted that, in these instances, the stenosis is moderate

If aortic insufficiency is present, the typical arterial syndrome is observed, and the pulse is larger and rapid

The sphygmogram shows a characteristic pattern with a notch in the ascending branch (*anacrotic pulse*) This pattern often has a stepwise rise or a plateau, the latter being the most common

Evolution and Prognosis. As mentioned above, a number of cases of aortic stenosis remain symptomless till late in adult life, when the first signs of insufficiency appear. Once cardiac insufficiency is present, the evolution is rapidly fatal

Sudden death, which may occur at any time, even in children or adolescents, is a constant threat to life and in itself aggravates the prognosis

AORTIC INSUFFICIENCY

Physical Signs Auscultation, as in cases of mitral stenosis, is of paramount importance in deciding whether or not aortic insufficiency is present Without a diastolic murmur, a diagnosis of aortic insufficiency cannot be entertained The diastolic murmur begins *with the 2d sound*, without interruption or gap, such as we find in the case of the diastolic rumble of mitral stenosis *Usually, the murmur is of* moderate intensity, soft, blowing, and "in decrescendo" during diastole. At times, the murmur can be very loud and be accompanied by palpable *thrill*, it may assume a *musical* or crackling quality These variations alone, taken without reference to the rest of the clinical picture, do not allow an evaluation of the severity of the lesion

The location of the murmur is variable The preferred site is the 2d right intercostal space at the sternal border However, the murmur can be heard only at the apex The murmur should be located between these two extremes, then followed along the left sternal border in an oblique line directed from above downward and from right to left, in the same direction as the regurgitant jet. The point of maximum intensity of the murmur corresponds approximately to the projection of the root of the aorta on the chest wall

As a rule, the diastolic murmur does not cover the 2d sound The latter may be *accentuated* at times, whereas in other cases it is *absent*. Should the 2d sound be absent, then the murmur may erroneously be considered as systolic.

An early-diastolic murmur is almost always due to aortic insufficiency. Exceptions do exist, but they are extremely rare Mention should be made at this point of the loud diastolic murmur, which can be found in patients with a large atrial septal defect and a dilated pulmonary artery. This is probably due to pulmonic insufficiency, even though catheterization may fail to confirm it.

The 1st sound may seem split, especially in young people This is probably due to the existence of *an opening snap of the aortic valve* which reinforces the second part of the 1st sound.[7] The diastolic murmur is variable in intensity and may even disappear for one or a few days Sometimes it is heard during an attack of rheumatic fever, sometimes only after a long time

The patients may have various arrhythmias: *extrasystoles, atrial fibrillation*, and *AV block*. The extrasystoles are evidence of increased excitability of the heart Atrial fibrillation seldom occurs in pure rheumatic aortic insufficiency. When it does, it is because there also is a mitral involvement, which was unnoticed. However, it is not unusual to observe it even in cases of cardiovascular syphilis or in cases with atherosclerosis of the aorta and coronary *heart disease Atrioventricular block is seldom* seen in rheumatic aortic insufficiency

Once the diagnosis of aortic insufficiency is made, the efficiency of the myocardium and the severity of the *hemodynamic disorder* should be evaluated In cases of insignificant, benign aortic insufficiency, there are no functional symptoms, and the diastolic murmur is the only finding. If the regurgitation is pronounced, even in the absence of functional signs, one can feel the apex as a hard ball which fills the palm of the hand, this is the "choc en dôme" The exploration of the arterial system is of the utmost importance.

The diastolic backflow of the blood markedly alters the arterial circulation If there is a small jet, the peripheral repercussions are minimal, the left ventricle is only slightly enlarged, and cardiac output is within normal limits If

[7] This opening snap of the aortic valve has been called "ejection sound" by Leatham The above expression is probably more correct because the vibration probably represents the accentuation of a normal sound phenomenon. *Editor.*

follow the 1st sound and occupy most of systole. This murmur was considered as evidence of a mitral insufficiency, but this is not always true, as shown by surgical and electrokymographic data. *Furthermore, mitral insufficiency, sometimes severe, may occur with mitral stenosis without giving rise to a murmur.*[3]

When the systolic murmur is in the midprecordial region at the left of the sternum, it is often related to severe dilatation of the right ventricle and is, therefore, of tricuspid origin. This murmur occasionally masks the auscultatory signs of stenosis and may be accompanied by a *triple rhythm (gallop)*.

A *soft, early diastolic murmur in decrescendo is often heard at the left of the sternum.* This has been interpreted as being due to relative pulmonic insufficiency (Graham Steell) or aortic insufficiency (Tandry and Routier). The latter might be due to traction exerted by a mitral leaflet on an aortic leaflet. Atrial fibrillation, atrial flutter, and supraventricular tachycardia often mask the auscultatory signs of mitral stenosis.

Right or left BBB occasionally occur in mitral stenosis Right BBB or interventricular block is more common.

Functional and physical signs do not permit an accurate evaluation of the degree of stenosis. Roentgenology, electrocardiography, and catheterization are very useful in this respect.

Among possible conditions which can simulate mitral stenosis, Graves' disease and tumors of the left atrium should be considered The latter, moreover, can be associated with mitral stenosis (ball-valve thrombus, myxoma)

The diagnosis of the evolutive stage, of the reactions of the myocardium, and of the degree of the stenosis cannot be established from the history and by auscultation alone Duroziez wrote, during the last century, that great progress would be made if one could see the heart through the chest and measure the pressure in the lesser circulation. These two aims have been reached through roentgenology and catheterization.

Treatment. Medical treatment cannot eliminate the mitral block and is limited to minimizing its harmful effects. It can also decrease or cure the acute or subacute rheumatic episodes, as well as the evolutive chronic process

[3] Left heart catheterization has confirmed these points. *Editor.*

The basis of every medical treatment is *rest* until the temperature has returned to normal and remained stable and regular. If, during an acute phase, the laboratory tests suggest a rheumatic recurrence, *corticosteroids* and *salicylates* are recommended.

Anticoagulant therapy is useful against "thromboembolic" phenomena. It should be used for prevention and not for treatment of current episodes. If there are good reasons to believe that the pulmonary infarcts are due to emboli originating in the legs, it may be necessary to ligate the saphenous or femoral veins, or even the inferior vena cava.[4]

MITRAL INSUFFICIENCY

Clinical Aspects. Before the first part of the twentieth century, mitral insufficiency was considered as the most frequent valvular lesion with a symptomatology rich in physical and functional signs. Up to that time, auscultation was about the only diagnostic method used by cardiologists, and since Marey (1863) developed his theory of murmurs, the apical systolic murmur was held as evidence of regurgitation through the mitral valve. At the turn of the nineteenth century, Potain stated that "not every apical systolic murmur represents a mitral leakage"; some of them, the softest, may be due to cardiac excitement, others may be of extracardiac origin. This last category is regarded today as extremely rare. At any rate, nowadays, mitral insufficiency is considered to occur less frequently than previously. Isolated instances are rare; practically, insufficiency is nearly always associated with stenosis because the inflammatory process which causes narrowing also alters the borders of the leaflets, thus permitting a backflow of blood into the left atrium. Usually, the leakage is insignificant, but in some instances it may be important, and its degree should be exactly determined before suggesting corrective surgery In the light of modern cardiology, a definite diagnosis of mitral insufficiency cannot be made only by auscultation. Electrocardiography, fluoroscopy, and left heart catheterization are needed for a correct evaluation.

[4] The role of *digitalis*, the use of *diuretics*, *diet*, and the various measures useful in congestive failure will be discussed in other parts of this book (Part 19). Surgical treatment will be discussed later, in this part. *Editor.*

origin *cannot be absolutely* ruled out because syphilis may follow rheumatic fever, so that both diseases occur in the same subject. Then syphilis causes additional lesions of the aortic valve plus invasion of the aortic wall, while a mitral lesion of rheumatic nature frequently exists. The existence of *intraventricular conduction disturbances* is seen more frequently in syphilitic heart disease but is not exclusive of this condition. *Acute pulmonary edema,* when present in young patients, is more suggestive of a rheumatic origin.

An *atherosclerotic process* is a frequent cause of aortic insufficiency. Clinically, the diagnosis is based on the typical diastolic murmur, indicating the valvular involvement. The symptoms due to this type of insufficiency are minimal, and the blood pressure is only slightly affected. This form may be found in old persons with or without precordial pain, or in cases of presenile atherosclerosis having a rapid evolution, or in cases of arterial hypertension. There was a time when all these patients were submitted to antisyphilitic treatment, in spite of the advanced age, negative history, and negative serologic tests. Greater knowledge of cardiovascular sclerosis has permitted the separation of these cases from those with syphilis.

In addition to the three mentioned causes, there are other, *rare or exceptional causes.* In the young infant, if a minimal attack of rheumatic fever can be ruled out, *a congenital bicuspid aorta* should be considered. This possibility is the most likely if other malformations are present, particularly coarctation of the aorta.

A *thoracic trauma* or a *violent muscular strain* may play a role in acquired aortic insufficiency. Both should be kept in mind in *medicolegal evaluations,* but it should be remembered that these factors act only on an already damaged aorta and usually only in adults or old people, where a "latent state" of aortic lesions already exists. The onset of the diastolic murmur in these patients is sudden, usually it is very loud, musical or cracking in quality, and at times audible to the patient. There may be a *palpable diastolic thrill.*

A similar murmur with sudden onset may appear in *rupture of the aorta,* a rare accident which usually occurs in hypertensive patients. After a short period of shock, these patients rapidly die. Very seldom does the patient recover from the accident, and then the left ventricle presents a severe dilatation. Survival is more common in the case of an *aortic tear (incomplete rupture).* The aorta usually tears in its supravalvular portion, with possible eversion of a *semilunar cusp.*

Severe insufficiency is found in cases where this valvular disturbance is associated with *Roger's disease.* Apparently, a scarring process originating in the interventricular foramen reaches a sigmoid valve and deforms one of the cusps.

During the course of *bacterial endocarditis,* aortic insufficiency may appear because of damage to the cusps by vegetations. *Tuberculosis* may localize over the aortic valve and cause an aortic insufficiency which, being associated with fever, may simulate *bacterial endocarditis.* This, however, is extremely rare.

Finally, it should be mentioned that an aortic diastolic murmur can be heard in cases of severe left ventricular dilatation. This is due to a *functional aortic insufficiency,* so-called because, on autopsy, *no alterations of the valves* or of the initial portion of the aorta can be found. However, the water test under conditions of physiologic pressure reveals the existence of a backflow into the ventricle. The extreme left ventricular dilatation abolishes the function of the subaortic muscular cushion, so that the cusps do not close in diastole.

Prognosis. Two factors are important in the prognosis: the severity of the hemodynamic disturbance and the presence of an inflammatory process in evolution.

HEMODYNAMIC DISTURBANCE. The more significant the backflow, the more severe the left ventricular overload. Systolic hypertension and dilatation of the left ventricle occur at the same time. As a consequence, the arterial peripheral syndrome appears. Thus, the degree of aortic insufficiency is *one* of the factors in the prognosis of the disease.

INFLAMMATORY PROCESS IN EVOLUTION. In contrast to mitral stenosis, *aortic insufficiency is not evolutive.* Not infrequently, patients with aortic insufficiency of rheumatic origin may *reach old age.* On the contrary, in luetic aortitis, the aortic insufficiency is but one stage of evolution. Again, in the course of atherosclerosis, aortic insufficiency is only part of the picture and is not proportional to the severity of the sclerotic process. In conclusion, aortic insufficiency in itself is not an evolutive proc-

follow the 1st sound and occupy most of systole. This murmur was considered as evidence of a mitral insufficiency, but this is not always true, as shown by surgical and electrokymographic data. *Furthermore, mitral insufficiency, sometimes severe, may occur with mitral stenosis without giving rise to a murmur.*[3]

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Treatment. Medical treatment cannot eliminate the mitral block and is limited to minimizing its harmful effects. It can also decrease or cure the acute or subacute rheumatic episodes, as well as the evolutive chronic process.

The basis of every medical treatment is *rest* until the temperature has returned to normal and remained stable and regular. If, during an acute phase, the laboratory tests suggest a rheumatic recurrence, *corticosteroids* and *salicylates* are recommended.

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[3] Left heart catheterization has confirmed these points. *Editor.*

[4] The role of *digitalis*, the use of *diuretics*, *diet*, and the various measures useful in congestive failure will be discussed in other parts of this book (Part 19) Surgical treatment will be discussed later, in this part *Editor.*

line is pushed back by a strong thrust of the chest to the right. Such systolic pulsation is to be distinguished from that transmitted to the right hypocondrium through the abdominal wall In aortic insufficiency, the liver may pulsate at every aortic pulsation. For diagnosis of tricuspid insufficiency, there should be a strong systolic thrust of the chest, as shown by Dressler. At times, the timing of the hepatic pulsations is different: the pulsations are actually *presystolic,* owing to venous engorgement plus strong right atrial contractions A hepatic tracing, together with an ECG, will solve any doubt as to the timing of the hepatic pulsations.

Functional Signs. Tricuspid insufficiency, *both permanent and transitory, represents an* aggravation of a preexisting heart disease upon which it *develops, the functional signs are* evidence of this aggravation and are similar to those of heart failure (severe dyspnea, anasarca, etc).

Evolution. When tricuspid insufficiency disappears in a short time with rest and treat*ment, one is entitled to think that it is* "functional," namely, due to dilatation of the right *ventricle,* while the tricuspid valve is not affected. On the other hand, if the tricuspid insufficiency persists after therapy, in spite of *hemodynamic readjustments, then one is en*titled to regard the insufficiency as being "organic" and due to a structural lesion of the tricuspid valve.

Long survival of cases of mitral stenosis complicated by tricuspid insufficiency has often been observed Even though the cardiac signs seem to lessen and become stabilized, hepatic signs develop and progressively increase until death of the patient. In other words, the patient ceases to be a cardiac and becomes a hepatic case The *dyspnea decreases, the evidence of cardiac insufficiency* becomes less apparent, but liver cirrhosis de*velops with ascitis, which requires* more and more frequent paracentesis, and the final outcome is cachexia with severe jaundice Long before the cirrhosis becomes manifest, the hepatic enlargement subsides because of increasing connective tissue and decrease of vascular space.

always present in patients with a congenital lesion.

In the adult, *syncope on exertion* may occur as well. The mechanism of such a paroxysmal attack is *relative cerebral ischemia*, due to the low ejection in the aorta. When exertion requires an increase of aortic flow, the disproportion becomes manifest and cerebral ischemia occurs.

For the same reason, *exertional precordial pain* is common in adults while it is seldom present in children. Precordial pain in a young adult should lead to suspicion of aortic stenosis. These attacks of pain are due to *coronary insufficiency*, again resulting from poor aortic flow. However, another factor should be taken into consideration: organic lesions of the aortic orifice may spread and lead to calcification in a region which has multiple nervous endings.

In the old-age group, syncope and precordial pain have less value for diagnosis because they may exist independently, as a result of coronary and cerebral vascular lesions.

The *functional pulmonary signs* represented by *exertional dyspnea, paroxysmal nocturnal dyspnea,* and *acute pulmonary edema* reflect the inability of the left ventricle to empty itself Thus, they are evidence of left ventricular failure, secondary to aortic stenosis As such, they usually appear late They indicate the terminal stage of evolution, which then progresses rapidly to a fatal outcome Another possible outcome of aortic stenosis is *sudden death*. a prolonged syncope without recovery

Physical Signs. *Auscultation* reveals an important sign that is easy to detect, a *systolic murmur* at the 2d right intercostal space This murmur is loud, harsh, and rough It is usually a grade IV to VI murmur It radiates along the vessels of the neck, especially on the right side, to the right supraclavicular region and to the suprasternal notch

Fluoroscopy shows that the point of maximum intensity of the murmur corresponds to the initial part of the ascending aorta A very important finding is that this murmur is *not* followed by a 2d sound The *disappearance of the 2d sound* is particularly apparent in the 1st right interspace, where the pulmonic component is poorly transmitted. Thus, for every cardiac beat, there is a loud systolic murmur followed by a silence.

The loudness of the murmur and its relatively superficial production also cause low-frequency vibrations which are felt by the palm of the hand over the point of maximum intensity. This is the *systolic thrill*, which is palpated in over 50 per cent of the cases Exploration of the 2d right intercostal space with the tip of the fingers may reveal even a minimal systolic thrill. The presence of a thrill in itself is not an indication of an organic lesion, but rather that of low-frequency vibrations, often below the threshold of auscultation[6] These vibrations are not exclusive of an organic lesion because they may be found even in cases with "relative" stenosis.

The finding of a systolic murmur and thrill and the absence of the 2d sound is typical in any case of isolated aortic stenosis, whatever the etiology. If aortic insufficiency is associated, then a diastolic murmur of lesser intensity is also present.

Soulié and Chiche have studied cases with associated aortic and mitral stenosis They point out that they may remain ignored until the development of cardiac failure, which then has a rapid evolution.

Some authors described *functional mitral insufficiency* in cases of aortic stenosis as a result of left ventricular dilatation. The diagnosis was based on the finding of a loud apical systolic murmur, which would substitute the harsh systolic murmur of the base. As a matter of fact, often aortic stenosis causes a systolic apical murmur radiating to the axilla, at times accompanied by a thrill, while, over the aorta, there is only a faint murmur or no murmur. The absence of the 2d aortic sound may then represent an important clue

The author is not in favor of the concept of "relative mitral insufficiency" because the loud apical systolic murmur may be caused by eddies which form in the dilated ventricle which empties itself with difficulty. Actually, this mitral insufficiency is not revealed by the various methods of investigation, including heart catheterization

Sphygmography. Blood pressure *is usually low Pulse pressure is low* while the diastolic pressure is normal. The amplitude of oscillations, revealed by an apparatus of Pachon, is decreased. There are, however, occasional cases with *arterial hypertension*. It is usually

[6] Graphic tracings reveal that the palpable vibrations are usually in the auditory range (between 75 and 200 cps). *Editor*

line is pushed back by a *strong thrust* of the chest to the right. Such systolic pulsation is to be distinguished from that transmitted to the right hypocondrium through the abdominal

systolic thrust of the chest, as shown by Dressler. At times, the timing of the hepatic pulsations is different: the pulsations are actually *presystolic*, owing to venous engorgement plus strong right atrial contractions. A hepatic tracing, together with an ECG, will solve any doubt as to the timing of the hepatic pulsations.

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Evolution. When tricuspid insufficiency disappears in a short time with rest and treatment, one is entitled to think that it is "functional," namely, due to dilatation of the right ventricle, while the tricuspid valve *is not affected*. On the other hand, if the tricuspid insufficiency persists after therapy, in spite of hemodynamic readjustments, then one is entitled to regard the insufficiency as being "organic" and due to a structural lesion of the tricuspid valve.

Long survival of cases of mitral stenosis complicated by tricuspid insufficiency has often been observed. Even though the cardiac signs seem to lessen and become stabilized, hepatic signs develop and progressively increase until death of the patient. In other words, the patient ceases to be a cardiac and becomes a hepatic case. The dyspnea decreases, the evidence of cardiac insufficiency becomes less apparent, but liver cirrhosis develops with ascitis, which requires more and more frequent paracentesis, and the final outcome is cachexia with severe jaundice. Long before the cirrhosis becomes manifest, the hepatic enlargement subsides because of increasing connective tissue and decrease of vascular space.

the jet is significant and the stroke volume increases, the arterial system expands and retracts rhythmically, giving rise to an "arterial dance" of the peripheral arteries. On palpation, the large, bouncing *Corrigan pulse* is felt.

Duroziez, compressing with the stethoscope the femoral artery at the groin, described *a double murmur*, a sign which was named after him.

The alterations of the blood pressure are proportional to the abnormal hemodynamics. There is a *drop of the diastolic pressure*, which may be absolute or relative (if there is hypertension). The systolic pressure is usually elevated because of increased stroke volume. Because of this, the *pulse pressure is increased*. The above alterations are in proportion to the severity of the regurgitation.[8] The tracing obtained with a sphygmograph reveals the characteristic changes of the pulse as they are felt on palpation.

Functional Signs. The excitability of the nervous system, including the centers of the cortex and midbrain and the sympathetic centers, is modified as a result of the abnormal hemodynamics When the peripheral vascular phenomena reach a certain point, increased excitability of the nervous system becomes manifest. The patient with aortic insufficiency is often uneasy, anxious, impatient, and restless, he is pale but flushes easily Attacks of *acute pulmonary edema* may be brought on by exertion or emotion.

Palpitation is frequent, usually because of the extrasystoles The latter are often ventricular but may be atrial.

Precordial pain is part of the usual complaints.

Whatever the etiology, the arterial system is under a continuous strain, which hastens atherosclerosis of the aorta and the coronary arteries.

Diagnosis. A soft diastolic murmur at the base of the heart is definite evidence of aortic insufficiency. Even if it is localized at the apex, no error is possible with mitral stenosis on account of the phase, timbre, and pitch of the murmur Pulmonic insufficiency will have to be excluded in cases of Eisenmenger's syndrome or large interatrial septal defect, where the diastolic murmur originates within the dilated pulmonary artery.

The etiology may be discussed in certain cases. The following causes are the most frequent.

1. Rheumatic fever represents the most common etiologic factor in the first twenty-five years of life.
2. Syphilis may occur in adults.
3. Atherosclerosis is typical of older people.

Aortic insufficiency, diagnosed before the age of 25, usually follows rheumatic fever, chorea, or scarlet fever. The same causes are frequently invoked in adults with no history of rheumatic episodes. Often, after the diagnosis of "aortic insufficiency of unknown etiology" is made, a typical rheumatic recurrence takes place, confirming the fact that the cardiac lesion was rheumatic.

Before admitting a rheumatic origin, one should make sure that tests for syphilis are negative. The existence of a mitral involvement should further be investigated. Then, the problem of whether or not aortic stenosis is also present should be discussed. A typical systolic murmur or, in its absence, aortic valvular calcification (fluoroscopy) and electrocardiographic evidence of systolic overload may suggest it. It is not unusual to observe conduction disturbances, prolonged P-R interval, or A-V block.

When the diagnosis is first made in a patient in late adult life, the rheumatic origin still remains a possibility, but its likelihood is minimal in the absence of a definite rheumatic history

In the past, it was stated that every aortic insufficiency with no proved cause should be regarded as syphilitic. Nowadays, this is not considered true, partly because syphilis is in marked regression. Syphilis can be admitted as the cause when the lesion has developed at the end of the fourth decade, cardiac integrity was known to exist before, there is a definite history and positive serologic tests Fluoroscopy or electrocardiography are of little help in establishing the cause.

In the case of cardiovascular syphilis, the heart is more involved than the aorta, and, on fluoroscopy, a large heart with barely visible contractions can be seen. If aortic insufficiency is accompanied by an aneurysm of the ascending aorta or the arch, syphilis is the most likely cause. But, even in these cases, the rheumatic

[8] Atherosclerosis of the aorta markedly increases the changes of the pulse and blood pressure. On the other hand, aortic stenosis decreases them. *Editor.*

any given change in flow rate produces a relatively larger change in the pressure gradient (Figs. 7-4 and 7-5). This is of particular importance when pressures are measured under conditions when the patient is not in a basal state, e.g., at operation or sometimes in the course of right or left heart catheterization. *Since there is no gradient normally, in clinical practice the measurement of pressures alone may be of value simply in detecting the presence or determining the absence of stenosis.*

When valvular regurgitation exists, the flow across the valve is the sum of the forward cardiac output and of the regurgitant flow. Both experimental and clinical observations indicate that regurgitant flow may be quite large and even greatly exceed the forward cardiac output. Therefore, *if regurgitant flow is neglected, the orifice size may be grossly underestimated.* [illegible] precise methods for measuring re- [illegible] orifice of a valve which is both stenotic [illegible] regurgitant *is not possible.* These considerations are of practical importance because of the coexistence of regurgitation and stenosis in most patients with valvular heart disease.

A significant prolongation of the time avail-

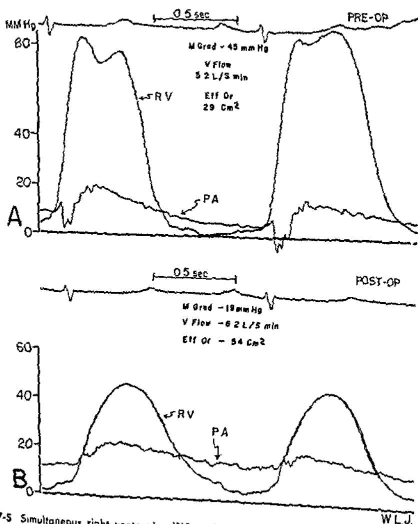


Fig. 7-5 Simultaneous right ventricular (RV) and pulmonary artery (PA) pressures obtained by direct needle puncture of these chambers in a patient with pulmonic stenosis at the time of operation under hypothermia A Before valvulotomy B After valvulotomy. *Stippled* areas represent pressure gradient across pulmonic valve. *M. Grad*, mean pulmonic valve gradient; *V. Flow*, valve flow rate in liters per systolic minute, *Eff Or.*, effective orifice size. Cardiac outputs were measured at the time of pressure measurement by the indicator-dilution method. (From Tanenbaum *et al.* New Eng. J of Med, 1958.)

ess nor can it alter the eventual evolution of the primary etiologic factor. Even when it is rheumatic in origin, subsequent recurrences do not aggravate a previous valvular involvement.

Medical Treatment. In view of the nonevolutive characteristic of the aortic insufficiency, the medical treatment consists of establishing a hygienic routine and correcting functional signs caused by the vascular syndrome.

In the case of insufficiency of syphilitic origin, antiluetic treatment is necessary. It should be carried out with caution in consideration of the age of the patient, the advanced degree of the disease, and the possible existence of myocardial and renal lesions.

TRICUSPID STENOSIS

Clinical Signs. The clinical signs of tricuspid stenosis are practically nonexistent because, on auscultation, there are signs due to alteration of other valves (mitral and aortic), which tricuspid stenosis eventually follows.[9] The inflammatory process involving the tricuspid valve is never isolated or primary, except in very rare cases.

Tricuspid stenosis is always secondary to mitral stenosis and is frequently accompanied by an involvement of the aortic valve, causing a *trivalvular stenosis.* Functional signs of cardiac insufficiency with a severe and refractory course are bound to suggest the possible tricuspid involvement during the evolution of a case of mitral stenosis. This is the more certain if, prior to this state, systolic pulsations of the liver were evident. Every case of tricuspid stenosis presents episodes of regurgitation during its evolution. These usually disappear when the stenosis becomes tighter.

No characteristic signs are found on fluoroscopy; only right heart catheterization suggests the diagnose of a clinically suspected tricuspid stenosis by showing a diastolic gradient between the two chambers of the right heart.

TRICUSPID INSUFFICIENCY

Pure isolated tricuspid insufficiency may exist but is exceptionally rare. Usually, it is a complication in the evolution of heart disease with right ventricular hypertension. Mitral stenosis is the most important cause, due to the fact that, beside right ventricular hypertension, there is the possibility of recurrent episodes of rheumatic fever, which may localize on the tricuspid valve.

Physical Signs. Inspection and palpation are the most valuable means of diagnosis, while the auscultatory signs may be practically absent. In the past, it was customary to describe a systolic murmur to the right of the sternum and near the xiphoid for analogy with the murmur of mitral insufficiency. To be sure, such a murmur is present whenever there is a large right ventricle, particularly if there is right ventricular failure, but this is no evidence of a regurgitant jet into the right atrium. Rivero Carvallo has particularly studied this murmur and showed that it increases with inspiration; this finding, though interesting from a physiologic standpoint, is not important because this murmur is rare in tricuspid insufficiency.[10]

Thus, only inspection and palpation may give evidence of tricuspid insufficiency. The *external jugular veins present large systolic pulsations.* This sign is far from being pathognomonic of organic tricuspid insufficiency, as it is present in any case of "functional insufficiency" of the tricuspid valve. As long as 50 years ago, MacKenzie considered the possibility of functional tricuspid insufficiency in the complete arrhythmia caused by atrial fibrillation. As this arrhythmia is frequently present in tricuspid insufficiency, a functional element may be added to the organic disorder.

These jugular pulsations are of diagnostic value if they are associated with the *characteristic thoracic pulsations* and especially with *systolic expansive pulsations of the liver.* For these signs to be present, it is necessary that the tricuspid regurgitation be significant, on the other hand, if these signs are absent, the leakage is hemodynamically insignificant.

In order better to evaluate the thoracic pulsations, the observer should stand at the foot of the bed and look at the chest of the patient in dorsal decubitus, in good light. At each beat, *the chest is thrust to the right with a seesaw movement which is opposed to the apical thrust.* A closed fist firmly placed over the right lower costal margin at the midaxillary

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cardiac output during exertion With further valvular narrowing, excessive elevation of the ... is at first prevented by fail-
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... cardiac output. Valvular stenosis can progress and be compatible with life as long as the cardiac output can fall farther and the pressure in the chamber proximal to the obstruction can rise farther. *In the absence of impaired contractility, the left ventricle can attain a systolic pressure as high as 300 to 350 mm Hg and the right ventricle a pressure as high as 200 to 250 mm Hg* In contrast, a mean left atrial pressure in excess of 35 to 40 mm Hg ordinarily results in the development of pulmonary edema. In patients with tricuspid stenosis, a right atrial pressure above 10 mm Hg is often accompanied by peripheral edema and ascites

With aortic or pulmonic valve stenosis and ventricular systolic pressure elevation, the increase in ventricular stroke work, as estimated by the product of stroke volume and aortic or pulmonary artery mean systolic pressure, requires a slight increase in ventricular end-diastolic pressure Persistent elevations of ventricular work may result in an impairment of ... f the function

... apparent, it may be related to rheumatic carditis, to a disproportion between the oxygen requirements of the heart and the oxygen availability, or possibly, to abnormalities in the structure of the contractile proteins (Olson). In any event, impaired ventricular contractility results in elevation of the ventricular end-diastolic (filling) pressure and therefore also in the corresponding atrial pressure Thus, the clinical picture associated with a stenotic valvular lesion is determined to some extent by the *contractility of the myocardium* It is of interest that Harvey *and her associates* (1955) have called attention *to a group* of patients with the clinical findings of mitral stenosis in whom the symptoms and hemodynamic findings were related primarily to myocardial failure rather than to valvular obstruction

Haddy and collaborators have observed in experimental mitral *stenosis that the* pulmonary venous pressure and the mitral valve *area* were inversely related. Furthermore, both the pressure gradient between the pulmonary artery and vein and the calculated pulmonary vascular resistance fell progressively as the mitral orifice narrowed and the pulmonary venous pressure rose. This may be explained by the increase in the cross-sectional area of the pulmonary vascular bed which accompanies distention, induced by the elevations of the pulmonary venous pressure. In contrast to these experimental observations, studies in patients with mitral valve disease have shown that both the pressure gradient between pulmonary artery and pulmonary "capillary" and the calculated pulmonary vascular resistance rise, sometimes to extremely high levels. These hemodynamic alterations are related to anatomic changes in the pulmonary vascular bed and result in a further elevation of right ventricular systolic pressure. The latter may limit right ventricular output and therefore flow across the stenotic mitral valve. In this manner, pulmonary vascular disease will tend to limit elevations of pulmonary capillary pressure

The experimental observation that myocardial oxygen consumption is primarily determined by the total tension developed by the myocardium (Sarnoff and Braunwald) helps to explain the frequent occurrence of symptoms of coronary insufficiency in patients with aortic stenosis. In such patients, in addition to the increased myocardial oxygen requirement, central aortic pressure is relatively low and oxygen availability is therefore limited by the relatively low coronary perfusion pressure.

INTRACARDIAC PRESSURE PULSES

While the demonstration of *an* elevated pressure gradient across a valve establishes the presence of stenosis, alterations in the contour of the intracardiac pressure pulses are also of considerable value in the recognition of valvular stenosis. In acute experimental mitral stenosis, the left atrium becomes distended and the left atrial contraction wave (A wave) *becomes tall. Thus is not* a particularly *prominent feature of the left* atrial pressure pulse in patients with mitral *stenosis* (Fig 7-7). *However, patients with tricuspid stenosis sometimes* exhibit enormous atrial contraction *waves* (giant A waves) with peaks that approach or *even exceed the magnitude of the right ven-*

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6

The hemodynamics of valvular regurgitation

EUGENE BRAUNWALD AND STANLEY J. SARNOFF

A full understanding of the pathophysiology of valvular regurgitation requires quantitative information concerning the alterations in circulatory pressures and flows brought about by such regurgitation This requires not only an understanding of the influence of known volumes of regurgitation on circulatory dynamics but, in addition, an appreciation of the influence of changes in various hemodynamic parameters on the volume of regurgitation, since the frequently changing states of activity in man obviously impose varying circulatory conditions Of primary importance is the fundamental difference between the pathophysiology of mitral and aortic regurgitation, since *in mitral insufficiency* the left ventricle ejects the regurgitant flow into a low-pressure system, while in aortic insufficiency it ejects the regurgitant flow into a high-pressure system (though it has a low pressure during the regurgitation, i e, in diastole).

Some insight into the importance of these interrelationships may be obtained in acute experiments in which mitral and aortic regurgitant flows can be directly metered and quantitatively varied The physiologic consequences of mitral regurgitation may be studied by permitting blood to flow from the left ventricle to the left atrium during systole through an external tube containing a flowmeter (Fig 7-8A) Aortic regurgitation may be similarly studied by permitting blood to flow from the aorta to the left ventricle during diastole through an external tube containing a flowmeter (Fig 7-8B) The influence of mitral regurgitation on aortic regurgitation may also be observed by inducing direct mitral regurgitation on preexisting known amounts of aortic regurgitation (Fig 7-8B).

MITRAL REGURGITATION

When mitral regurgitant flow is increased from zero to values in excess of twice the resting effective cardiac output, surprisingly modest changes in effective cardiac output, aortic pressure, and left atrial mean and ventricular filling pressures occur. Calculated *total peripheral resistance* rises only slightly. In the presence of mitral regurgitant flows which approximate the dog's resting effective cardiac output, little depression of the effective left ventricular function curves[1] is observed It is also of interest that the increment in ventricular filling pressure required to provide any given increment of forward cardiac output substantially exceeds that which is required to produce a similar increment of mitral regurgitant flow That is, *at constant ventricular filling pressures, the left ventricle can eject substantially larger volume into the left atrium than into the aorta.*

If ventricular distensibility remains essen-

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The hemodynamics of valvular stenosis

EUGENE BRAUNWALD

HYDRODYNAMIC CONSIDERATIONS

The development of practical methods for the precise measurement of pressures in the cardiac chambers and great vessels adjacent to the valves and of blood flow across the valves has resulted in the present understanding of the hemodynamics of stenotic valvular heart disease. Such measurements have made it clear that the fundamental hemodynamic expression of functionally significant valvular obstruction is the presence of a *pressure gradient* across the stenotic orifice at the time when flow across the orifice takes place. It has been observed that, in the absence of anatomic obstruction, the normal cardiac output can pass across the heart's valves and develop a pressure gradient so small that it cannot be detected with present techniques. The application of hydraulic principles to the hemodynamics of valvular stenosis by Gorlin and Gorlin has not only focused attention on the interrelationships between effective valve orifice size, valve flow rates, and pressure gradients, but also has provided formulas for the estimation of effective orifice size in vivo

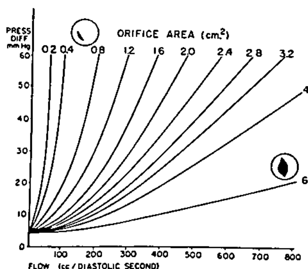


Fig. 7-4. Relationship between atrial diastolic pressure and mitral valve flow rate for mitral orifices ranging from 0.2 to 6 cm². A left ventricular diastolic pressure of 5 mm Hg is assumed. *(From Rushmer's Cardiac Diagnosis, adapted from Gorlin and Gorlin Am. Heart J. 1951.)*

When the flow of blood is laminar and other factors are constant, the flow rate is a linear function of the pressure gradient between any two points in the circulatory path. However, when blood flow is turbulent, as it is across stenotic heart valves during at least a portion of the cardiac cycle, greater energy losses occur and the flow rate is more closely proportional to the square root of the mean pressure gradient (Gorlin and Gorlin) In the presence of turbulent flow, the relationship between the pressure gradient and the flow rate across any given stenotic orifice may, therefore, be graphically depicted by one limb of a parabola (Fig. 7-4). From such considerations, it is apparent that a *doubling of the blood flow across a stenotic valve, as may readily occur during mild exertion, will require quadrupling of the gradient across the orifice.* Estimation of the severity of valvular stenosis by measurement of pressure gradients alone is not possible, since

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able for flow across stenotic valves occurs when obstruction is severe. Ventricular contraction is relatively more isometric than normal, and the duration of ejection is prolonged in the presence of stenosis of the semilunar valves. In the presence of tricuspid or mitral stenosis, ventricular filling can begin earlier than normal since the elevated atrial pressure serves to abbreviate the duration of isometric relaxation (Fig. 7-6). Similarly, the end-diastolic A-V pressure gradient permits ventricular filling to continue until the ventricular pressure reaches the level of the elevated atrial pressure (Braunwald et al., 1955). It is evident that, at any given level of the cardiac output, a prolongation of the time during which blood flows across a stenotic orifice results in lowering of the pressure gradient

Alterations in heart rate also modify the time during which flow across valves can occur (Braunwald et al., 1958) An increase in heart rate prolongs the total duration of ejection per minute and thereby prolongs the total time per minute available for flow across the semilunar valves. However, tachycardia abbreviates diastole and the time per minute available for ventricular filling At any given minute during cardiac output, therefore, tachycardia of itself will decrease the pressure gradient across the semilunar valves but will augment the gradient across the AV valves (Gorlin et al., 1951). The relationship between the duration of diastole and the end-diastolic left AV pressure gradient across the mitral valve in a patient with mitral stenosis is demonstrated by the fact that, when diastole is abbreviated, left atrial emptying is incomplete and a larger AV pressure gradient results.

PHYSIOLOGIC AND CLINICAL CORRELATIONS

Heart valves possess a large functional reserve area, since with normal flow rates, a reduction of more than 50 per cent of the normal cross-sectional area must occur before significant functional abnormalities result; reductions to 10 to 20 per cent of normal are compatible with life (Macdonald et al.). As stenosis develops, the laminar flow across the valvular orifice becomes turbulent during the period of rapid flow and produces a "stenotic murmur." It should be emphasized that a degree of obstruction which results in an easily audible murmur need not necessarily be accompanied by a pressure gradient nor by any other hemodynamic abnormality. When the obstruction becomes severe enough to be functionally significant, this is often manifested only in an abnormal pressure gradient, at this stage the cardiac output may be normal at rest, and elevation of the pressure gradient may accompany normal augmentation of the

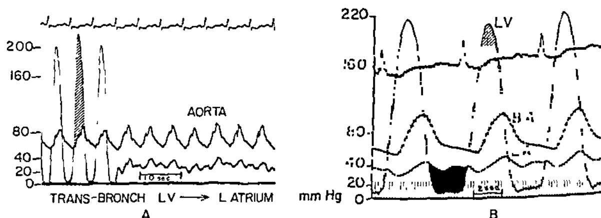


Fig 7-6. A. Pressures in the left atrium, left ventricle (LV), and central aorta from a patient with combined mitral and aortic stenosis Aortic pressure obtained by retrograde arterial catheterization Left heart pressures obtained by transbronchial left heart catheterization (4, 5). Lined area represents aortic valve gradient. B. Simultaneous pressures from the left atrium (LA), left ventricle (LV), and brachial artery (BA) obtained by transbronchial left heart catheterization in a patient with combined mitral and aortic stenosis The stippled area represents the mitral valve gradient and the lined area the aortic valve gradient. The simultaneous determination of cardiac output by the indicator-dilution method permitted calculation of effective orifice size of both valves. *(Reproduced by permission of the authors from Morrow et al. Circulation. 1957)*

The observation that the effect of any given regurgitant volume on left atrial pressure is a function of the filling pressure prior to the induction of regurgitation may be helpful in the interpretation of hemodynamic findings in clinical mitral insufficiency. With the heart operating on any given left ventricular function curve, its specific position on that curve is of importance. Further, the particular ventricular function curve on which the heart is operating will also substantially influence the filling pressure at which the ventricle is doing its effective stroke work. Thus, if the left ventricle is operating on a depressed function curve, that is, has an impaired myocardial contractility due to a disease such as rheumatic carditis, the *filling pressure and left atrial pressures will have to be higher to maintain any given level of effective stroke work*. Under such circumstances, the effect of any given mitral regurgitant volume will be to elevate left atrial pressure more than if the ventricular function curve were not depressed. An ancillary consideration is the rate of development of ventricular systolic pressure. These rates are lower in hearts with depressed function curves. As suggested by Wiggers, a "hypodynamic" systolic contraction would tend further to augment mitral regurgitation.

The increase of left atrial pressure which occurs with any given regurgitant stroke volume will also be a function of that point on the pressure-volume curve of the left atrium and pulmonary vascular bed occurring at that time. If, as has recently been suggested, changes in pulmonary vascular distensibility do occur with mitral insufficiency, such changes will also modify the extent of the rise in left atrial pressure. In addition, the *associated increase in pulmonary vascular resistance would further intensify the pulmonary hypertension*. This combination of circumstances may help to explain the clinical manifestations of right ventricular failure in patients with pure mitral regurgitation.

It is of considerable interest that the mitral regurgitant flows produced were as high as those observed and that they were associated with such small elevations of left atrial pressure since striking elevations of this pressure are observed when mitral valve injury is experimentally induced and also in the naturally occurring disease state in man. Further, if left ventricular hypertrophy is associated with mitral regurgitation in the absence of other myocardial disease, it might be anticipated that the volume of regurgitation which the ventricle can endure would be even greater than in the absence of such hypertrophy.

The observation of elevated left ventricular filling pressures in patients with pure mitral insufficiency, when viewed in the light of the above data, could be explained by the presence of (1) mitral regurgitant flows relative to cardiac output grossly in excess of those described above, (2) depressed left ventricular function curves due to myocardial disease, or (3) possible changes in ventricular distensibility secondary to myocardial hypertrophy. In this connection, it is of interest that observers, using the Korner-Shillingford method for the estimation of mitral regurgitant flow, found regurgitant flows averaging 165 per cent of the effective cardiac output in patients with predominant mitral regurgitation in whom left ventricular end-diastolic pressures were not elevated.

Wiggers and Feil demonstrated striking elevations of the left atrial V wave when aortic pressure was increased in the presence of mitral regurgitation.[2] As might be anticipated from their observations, with any given mitral regurgitant orifice, an increase in the resistance to left ventricular outflow, which in turn increases the systolic pressure gradient across the regurgitant orifice, produces an approximately parallel increase in mitral regurgitant flow with a reciprocal fall in forward flow.

Such augmentation of mitral regurgitant flow and the consequent striking elevation of the V wave[2] when resistance to aortic ejection is increased have also been observed in patients with mitral regurgitation when aortic pressure was elevated by norepinephrine infusion. This response has proved helpful as a diagnostic test for the presence of even mild degrees of mitral regurgitation which were not otherwise hemodynamically apparent.

It has recently been demonstrated that the oxygen consumption of the heart is determined largely, if not solely, by the tension-time index (mean aortic systolic pressure times the dura-

[2] Discussion of this point will be found in Chap 13, dealing with left heart catheterization. Editor

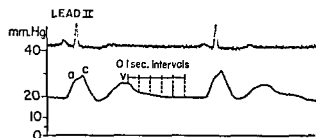


Fig. 7-7. Left atrial pressure pulse obtained by transbronchial puncture in a patient with pure mitral stenosis. The *a*, *c*, and *v* waves are indicated. The mean left atrial pressure is elevated, the *v* wave is not prominent, the pressure descent during the first 0.10 sec after the *v* wave is slow, and there is no evidence of diastasis. (*Reproduced by permission of the authors from Morrow et al. Circulation.* 1957.)

tricular systolic pressure (Killip and Lukas, 1957a). In the absence of mitral or tricuspid stenosis, rapid filling of the ventricle takes place during early ventricular diastole. Later in diastole, as more blood enters the already well-filled ventricle, both the ventricular and atrial pressures rise, during the period of diastasis or slow ventricular filling Mitral or tricuspid valve stenosis prevents rapid ventricular filling in early ventricular diastole, the atrial pressure drops slowly during early ventricular diastole and the y descent is gradual and prolonged (Fig 7-7). The slow ventricular filling in early diastole abolishes diastasis, and the atrial pressure therefore continues to fall until the subsequent atrial contraction It has been observed that patients with elevated left atrial pressures, in whom the left atrial pressure drop during the first 0 10 sec of the y descent is less than 40 per cent of the mean left atrial pressure and in whom diastasis is absent, have mitral stenosis as their predominant lesion at operation (Morrow et al., 1957).

The presence of pulmonic or aortic stenosis modifies the ventricular pressure pulse by producing a summit with a peak during midsystole instead of the normal plateau. Although the rate of pressure rise in the ventricle proximal to the stenosis is rapid, the pressure rises gradually in the vessel just distal to the stenois and peaks at the end of systole (Fig 7-6A). A prominent *anacrotic shoulder* or notch during early systole ushers in a series of *rapid systolic vibrations* in the central aortic or pulmonary artery pressure pulse. These vibrations are coincident with the murmur and apparently reflect the turbulent flow across the stenotic valve orifice. Left ventricular pulsus alternans is frequently observed in patients with acquired aortic stenosis. While the alternation may be detectable in the aortic or peripheral pressure pulse, its magnitude is markedly reduced.

SUMMARY

In summary, the hemodynamics of valvular stenosis have been considered from three points of view. The hydraulic effects of valvular stenosis are discussed with emphasis on the interrelationship between pressure gradients, blood flow across the valve, and those factors which regulate the duration of blood flow The hemodynamic effects of valvular stenosis on the myocardium are considered, and the importance of the contractility of the myocardium as a factor in determining the clinical picture associated with stenotic valvular heart disease is stressed. Finally, some of the modifications of the various pressure pulses produced by valvular stenosis are briefly reviewed.

constrictor response, diastolic coronary perfusion pressure would fall to levels even lower than those which were maintained. The constrictor response may be construed, therefore, as conferring a protective effect under such experimental conditions. Clinically, since cardiac output at rest is not generally decreased in patients with mild or moderate aortic regurgitation, there is no requirement for an increased peripheral vascular resistance. However, it might be anticipated that, as the severity of the regurgitant lesion progresses, effective cardiac output is depressed because of the inability of the ventricle to compensate further. As observed by Gorlin, patients with aortic regurgitation who develop left ventricular failure would appear to exhibit an elevated peripheral vascular resistance. Under such circumstances, increased peripheral vascular resistance may play an increasingly important role in the maintenance of arterial and coronary perfusion pressure.

The diastolic or coronary perfusion pressure is an important aspect of adequate oxygen availability to the myocardium, while as noted above, the tension-time index is thought to be the primary determinant of the requirement of the heart for oxygen. Thus again, unlike similar or even larger volumes of mitral regurgitation, aortic regurgitation may be expected to result in an increased oxygen requirement in the presence of a hemodynamic limitation of oxygen availability (low diastolic pressure). This view is consistent with the *clinical manifestations of myocardial ischemia (or coronary insufficiency) which are fairly frequently observed in patients with aortic regurgitation.*

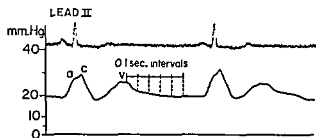


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The presence of pulmonic or aortic stenosis modifies the ventricular pressure pulse by producing a summit with a peak during midsystole instead of the normal plateau. Although the rate of pressure rise in the ventricle proximal to the stenosis is rapid, the pressure rises gradually in the vessel just distal to the stenois and peaks at the end of systole (Fig. 7-6A). A prominent *anacrotic shoulder* or notch during early systole ushers in a series of *rapid systolic vibrations* in the central aortic or pulmonary artery pressure pulse. These vibrations are coincident with the murmur and apparently reflect the turbulent flow across the stenotic valve orifice. Left ventricular pulsus alternans is frequently observed in patients with acquired aortic stenosis. While the alternation may be detectable in the aortic or peripheral pressure pulse, its magnitude is markedly reduced.

SUMMARY

In summary, the hemodynamics of valvular stenosis have been considered from three points of view. The hydraulic effects of valvular stenosis are discussed with emphasis on the interrelationship between pressure gradients, blood flow across the valve, and those factors which regulate the duration of blood flow The hemodynamic effects of valvular stenosis on the myocardium are considered, and the importance of the contractility of the myocardium as a factor in determining the clinical picture associated with stenotic valvular heart disease is stressed Finally, some of the modifications of the various pressure pulses produced by valvular stenosis are briefly reviewed.

tricular block) is the result of myocardial damage It may become permanent. Transitory evidence of *right ventricular hypertrophy* may be found

In 50 per cent of the cases, *alterations of the S-T trace and of the T wave* occur They are due to pericarditis, rheumatic lesion of the coronaries (Grenet, 1946), or lesion of the myocardium (de la Chapelle). Autonomic stimuli may concur in the production of these changes (Alzamora, 1952), which indicate a severe prognosis, if they persist.

A sign in the ECG which has been considered important in the evaluation of the course of rheumatic fever is *prolongation of electrical systole* (*Q-T interval*). An exact measure of the electrical systole is not always easy: the end of the T wave may be poorly defined, the T wave may be fused with the U wave (Lepeschkin, 1952). Possible other causes of prolongation of Q-T should be kept in mind: emotion, hypertension, heart failure, quinidine, pulmonary embolism, hypocalcemia, exercise On the contrary, other factors may shorten Q-T· digitalis, cortical steroids, salicylates, pericarditis In spite of these considerations, the value of a prolongation of Q-T is still remarkable, particularly because it has been said that it can be the only sign of evolution of the disease while all others have become normal (Taran, 1947) Prognostic significance has also been attached to this sign in the ECG (Taran, 1951) On the other hand, the Q-T interval remains within normal limits in many cases of rheumatic fever (Craige, 1950)

In summary, acute rheumatic fever is accompanied often by electrocardiographic abnormalities, the most frequent of which are changes of the P-R and S-T intervals and of the T waves These alterations, even though important for diagnosis and prognosis, are not specific On the other hand, cases with an active rheumatic process proved by auricular biopsy can show a normal ECG (McNeely, 1953)

MITRAL STENOSIS

Sir Thomas Lewis (1913) claimed that the ECG of mitral stenosis is often so characteristic that the diagnosis of the valvular lesion can be made from the tracing. Actually, the electrocardiographic changes appear later than the acoustic and radiologic signs (Parkinson, 1946). In certain cases, the ECG was unchanged for more than 10 years (Rasmussen, 1951). Therefore, an early diagnosis of mitral stenosis can hardly be made on the basis of the ECG. On the other hand, once

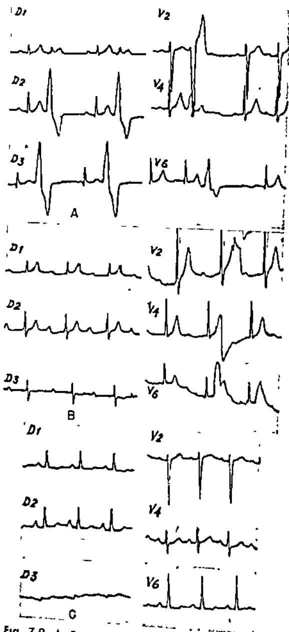


Fig 7-9 A. Patient with acute rheumatic fever; no digitalis, run of premature contractions with a bigeminal rhythm. P-R interval, 0 24 sec B Patient with rheumatic myocarditis Grade 1 AV block P-R interval, 0 44 sec C. Patient with acute rheumatic fever and rheumatic myocarditis. The first ECG showed important alterations of repolarization which disappeared in the ECG taken 3 weeks later.

tially unchanged, these observations are best explained by more complete systolic emptying *when mitral regurgitation is present.* This is facilitated, not only by the high pressure gradient between ventricle and atrium, but also by the continuation of regurgitation during protodiastole and isometric relaxation, as shown by Wiggers. It is clear, however, that the primary compensatory mechanism of more complete systolic emptying is gradually exhausted when mitral regurgitant stroke volumes increase further. Under such circumstances, an *increase of the end-diastolic ventricular volume must occur* This is indicated, not only by the slight depression of the ventricular function curve which has been noted above, but also by the progressive depression of the ventricular function curve as mitral regurgitant volumes are further augmented.

The effect on left atrial Z point pressure (left ventricular filling pressure) of progressively increasing mitral regurgitant flow was examined at two different forward cardiac outputs at comparable aortic pressures and heart rates. When forward cardiac output was maintained at a low level, left atrial pressure was 3.5 cm H_2O before mitral regurgitation was induced, and 4.74 liters/min of regurgitation raised the left atrial pressure 4 5 cm H_2O. In contrast, when forward cardiac output was maintained at a higher level and left atrial Z point pressure was 10 cm H_2O before mitral regurgitation was induced, 4 09 liters/min of regurgitation raised the left atrial pressure 11 5 cm H_2O.

It was consistently observed that the higher the ventricular filling pressure prior to mitral regurgitation, the greater was the subsequent elevation of filling pressure and left atrial pressure produced by any given amount of regurgitation.

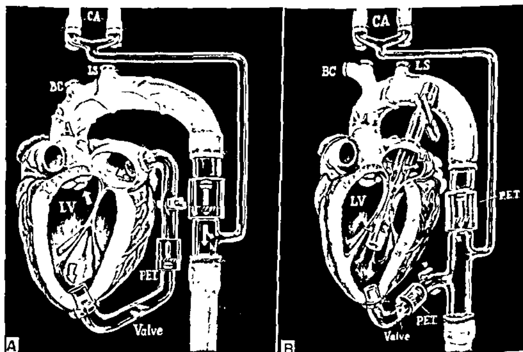


Fig. 7-8. A Schematic diagram showing the experimental preparation for producing and recording ventriculo-atrial regurgitation while simultaneously recording forward cardiac output. *PET*, Potter turbine flowmeters; *BC*, brachiocephalic artery, *LS*, left subclavian artery, *CA*, carotid arteries, *A*, aorta, *LV*, left ventricle A check valve in the regurgitant path permits flow only during systole *The screw clamp is used to vary regurgitant volume. A second screw clamp (not shown)* applied to the aortic tubing permits graded increases of resistance to left ventricular outflow. B. Schematic diagram showing preparation for producing aortic–left ventricular regurgitation, including check valve and flowmeter for the recording of regurgitant flow during diastole. Second flowmeter records total left ventricular output (minus coronary flow) A perforated tube placed in the left ventricle *through the left atrial appendage and mitral valve to superimpose mitral regurgitation* on metered aortic regurgitation. Effective cardiac output = total minus regurgitant flow. *LA*, left atrium; *LV*, left ventricle; *A*, aorta; *BC*, brachiocephalic artery, *LS*, left subclavian artery; *CA*, carotid arteries Screw clamp on regurgitant tubing allows control of volume of regurgitation.

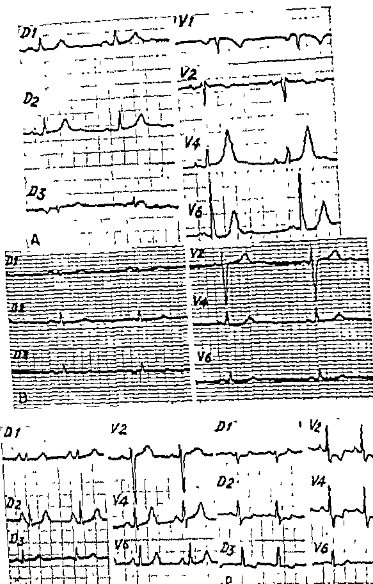


Fig. 7-10 A Pure mitral stenosis in a 50-year-old man. Pulmonary capillary and pulmonary arterial pressures, normal (mean pulmonary capillary pressure, 8 mm Hg, pulmonary artery, systolic, 23; diastolic, 11) The ECG shows neither the pattern of right ventricular overload, or augmented P wave Notching of the P wave is present B. Pure mitral stenosis in a 35-year-old woman. Severe exertional dyspnea. Pulmonary capillary pressure greatly increased (mean pulmonary capillary pressure, 24 mm Hg). Pulmonary artery pressure, moderately augmented (systolic, 45; diastolic, 20, mean, 30 mm Hg) The ECG shows neither right ventricular overload nor a high P wave. However, the P wave is like a notched plateau. C Pure mitral stenosis in a 28-year-old woman. Severe exertional dyspnea with cough and hemoptysis on exertion. Pulmonary capillary pressure very high (mean, 30 mm Hg) Pulmonary artery pressure markedly increased (systolic, 63; diastolic, 37; mean, 50 mm Hg). The ECG does not show signs of right ventricular overload (the pressures in the pulmonary artery are in the neighborhood of the threshold where modifications of the QRS appear). On the other hand, the marked increase of amplitude of the P wave indicates pulmonary arterial hypertension D Severe pure mitral stenosis (with marked dyspnea) in a 38-year-old woman. Pulmonary artery pressure extremely elevated (systolic, 120; diastolic, 55; mean, 82 mm Hg). The ECG shows a marked right ventricular overload; QRS more than 90°, high voltage of R in V_2 with abnormal repolarization.

tion of systole) and is independent of the stroke volume except in so far as the latter changes the duration of the tension state developed by the myocardium. The fact that no significant change in the tension-time index occurs with mitral regurgitation strongly suggests that the oxygen consumption of the left ventricle is not substantially increased by large volumes of mitral regurgitation and may help to explain the clinical observation that precordial pain is relatively rare, even in patients with severe mitral insufficiency.

AORTIC REGURGITATION

Acutely produced aortic regurgitation results in a hemodynamic pattern which consistently stands in sharp contrast to that produced by similar or even greater volumes of mitral regurgitation As aortic regurgitant flow is increased, effective cardiac output decreases substantially. This decrease is accompanied by a widening of the pulse pressure and a lower diastolic pressure. Mean pressure is usually slightly diminished. Systolic aortic pressure usually arises but does not always do so. Calculated total peripheral resistance rises markedly. *Left ventricular end-diastolic pressure rises to high levels,* while mean left atrial pressure exhibits only a slight elevation. Thus, in acutely produced aortic regurgitation, wide discrepancies between left ventricular and left atrial pressures are observed in end diastole. Again, in contrast to mitral regurgitation, aortic regurgitation is accompanied by severe depression of the effective left ventricular function curve. In contrast to the more complete systolic emptying of mitral regurgitation, the increased total stroke volume of aortic regurgitation is ejected into the aorta in which the pressure is high. It appears that the *increased stroke volume of aortic regurgitation is chiefly accomplished by an increased end-diastolic ventricular volume.*

Of considerable interest in the appraisal of the hemodynamic consequences of valvular regurgitation is the interrelationship between the regurgitant lesions of both valves. When mitral regurgitation is added to aortic regurgitation, even though the aortic regurgitant flow becomes slightly diminished, effective cardiac output falls farther from its already depressed level. Simultaneously, left ventricular end-diastolic pressure falls from its high level while mean left atrial pressure rises, thus diminishing the discrepancy that was present between them when the mitral valve was competent. In the presence of aortic regurgitation alone, it is clear that a competent mitral valve must close partially or completely well before the onset of ventricular systole; else the late diastolic reverse pressure gradient between ventricle and atrium could not develop Furthermore, in the presence of aortic regurgitation, compromising the competence of the mitral valve induces a further elevation of left atrial pressure and a fall in left ventricular end-diastolic pressure. This decrease in left ventricular end-diastolic pressure (and presumably fiber length) results in a further diminution of stroke work and cardiac output from the already depressed levels Under such circumstances, the competent mitral valve may be thought of not only as a secondary resistance to regurgitant flow from the aorta, but also as a means of protecting the pulmonary vascular bed from elevated pressures, while permitting the left ventricle to achieve a high enough end-diastolic pressure for the discharge of a more adequate stroke volume than would otherwise be the case.

The large volumes of aortic regurgitant flow that were observed in these experiments do not appear to be unrealistic in terms of the clinical counterpart of this lesion. In clinical studies on patients with severe aortic insufficiency, when dye was introduced into the aorta at or below the level of the diaphragm, it was observed to regurgitate retrograde to the innominate artery as indicated by its photometric detection in the ear promptly after the aortic injection. The studies of clinical aortic regurgitation by the method of Korner and Shillingford would also appear to be consonant with this view. Further, with time for the development of compensatory hypertrophy, it would be expected that the naturally occurring lesion might result in a left ventricle that could endure larger aortic regurgitant volumes than when the lesion is acutely induced as was done in these experiments.

The observed increase in calculated peripheral vascular resistance which accompanied the fall in effective cardiac output when aortic regurgitation was acutely induced *represents the activity of pressoreceptor regulation in maintaining arterial pressure.* Without such a

brillation is rather frequent (Jouve, 1948).

In isolated mitral insufficiency with a *significant regurgitation*, the electric axis is deviated *to the left* in one-third of the cases, and signs of left ventricular overload are usually present (Bridgden, 1953). Therefore, if a case of mitral stenosis presents left axis deviation, significant regurgitation is to be suspected, even in the absence of an apical systolic murmur. In mitral insufficiency, concomitant signs of right ventricular overload are frequently seen in the precordial leads (Heller, 1956) The critical level of increased pulmonary resistance causing right ventricular hypertrophy is higher than for isolated mitral stenosis. On the contrary, right axis deviation (aQRS of 90°) associated with a delayed intrinsicoid deflection in leads V_1 and V_2 is common, in cases with double mitral defect and even with severe regurgitation (Cabrera, 1949).

In conclusion, left ventricular overload is frequently present in the rather rare cases of pure mitral insufficiency, but combined ventricular overload in the precordial leads may be observed in them In mitral valve disease, left ventricular overload indicates a significant regurgitation, but the latter may be present even if there is a right ventricular overload

AORTIC STENOSIS

Aortic stenosis usually causes a systolic overload of the left ventricle Relative or absolute coronary insufficiency is not uncommon The ECG tracing may be within *normal limits* (Davies, 1949), but usually significant alterations can be detected (Fig 7-11)

Left ventricular hypertrophy frequently causes a marked left axis deviation of the QRS (Kilaidonis, 1949), but an axis indicating a vertical heart can be seen (Kiloh, 1950). The axis of T is frequently deviated to the right (Balestier, 1949) The T wave may be negative only in lead I, or in leads I and II, and occasionally in all the three standard leads A *negative T wave* is a more frequent finding when the weight of the heart is severely increased (Dry, 1939) In the left precordial leads, the R wave usually presents high voltage (Fig. 7-11) Changes of the T wave in cases of calcific aortic stenosis are frequently (more than 50 per cent, Tourniare) associated with alterations of the S-T segment These have been considered evidence of a severe myocardial lesion (Berk, 1938). On the other hand, they might be due *to coronary insufficiency*, and we should remember that coronary stenosis is frequent in these cases (Horan, 1948). The *concordant inversion of* the T wave (leads I, II, and III) is considered characteristic of aortic stenosis as compared to the opposite changes of the T wave in leads I and III, due to the most common type of coronary insufficiency (Tourniare, 1947).

Calcific aortic stenosis is the valvular lesion most frequently associated with *left BBB*. Even in the absence of complete BBB, the duration of QRS and the delay of the intrinsicoid deflection in the left precordial leads are greater in aortic stenosis than in aortic regurgitation (Kilaidonis, 1949)

In addition to intraventricular conduction disturbances, various degrees of AV block should be considered (Davies, 1949). In cases of calcific stenosis, this block *has been explained* with an extension of the process to the conduction system (Boas, 1935)

Atrial fibrillation has been reported in cases of aortic stenosis but is rather rare (Contratto, 1937).

AORTIC INSUFFICIENCY

The diastolic overload of the left ventricle caused by the aortic regurgitation causes *a shift to the left of the axis of QRS. High voltage* of R in the left precordial leads with a slight *delay of the* intrinsicoid deflection is common. Nevertheless, there may be no change of the axis in young patients. In these cases, there is a negative T wave *in leads II, III*, and aVF, and the interpretation of "left ventricular overload" can be made only on the basis of the precordial leads

In the rheumatic form, the mean electrical axis is usually between −90 and +90; *in the* syphilitic type of lesion, the aT is more frequently deviated to the right (Friedland, 1949) Alterations *of the* S-T segment and the T wave in lead I should be *mentioned*, particularly in young individuals having attacks of precordial pain without evidence of coronary lesions (Lequime, 1945) Inversion *of the* T wave in the left precordial leads *is* also seen quite often.

The presence of *positive T* waves of high voltage in the left precordial leads *has* been claimed as being characteristic of diastolic

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The electrocardiogram in rheumatic fever and rheumatic heart disease

JEAN LEQUIME AND J. HANSON

ACUTE RHEUMATIC FEVER

Long ago (Cohn, 1924), the electrocardiogram was studied as a guide in the follow-up of rheumatic patients However, as in other biological tests, the ECG changes are not specific, as a matter of fact, only one-third of patients with acute infections or, in general, fever may show changes of the T wave (de la Chapelle, 1954) or the P-R interval (Sanghir, 1956) Thus, the ECG changes observed during acute rheumatic fever are the expression of nonspecific myocardial damage. Therefore, frequent tracings are necessary in order to discover them A temporary *prolongation of the P-R interval* may be brought about by increased vagal tone (Bruenn, 1937), even though it is a frequent sign during acute rheumatic fever Various degrees of *AV block* may be found (Fig 7-9) A first-degree AV block should be correlated with the age of the patient and the cardiac rate, because the normal range (0 12 to 20 sec) includes values which are definitely abnormal in young people with tachycardia. If the P-R interval is calculated according to the table of Lepeschkin (1942), it is found prolonged in more than 50 per cent of the cases of acute rheumatic fever This conduction disturbance may be due in some cases to vagal reflexes originating in the myocardium, the aorta, or the lungs, affected by the inflammatory process (Altschule, 1939). A persisting, long P-R interval may even indicate a predisposition to atrial fibrillation (Altschule, 1939). The role played by autonomic stimuli can be shown by the fact that, in patients with acute rheumatic fever, the compression of the carotid sinus prolongs the P-R interval beyond physiologic limits, even if it was normal at the onset of the test (Foscarini, 1949). In spite of the autonomic element in the genesis of these first-degree AV blocks, persistence of a long P-R interval in infants indicates a severe prognosis (Joly).

Changes of the P wave may occur. This wave may become flat and even inverted in leads II and III (Sampson, 1946).

Even though *sinus tachycardia* is the most common disturbance, a *sinus bradycardia* (absolute or relative) may appear. This disturbance is due to high vagal tonus and may have a prognostic value (Zimdhal, 1952). *Wenckebach periods* occur frequently: the P-R interval then becomes progressively prolonged until AV block occurs, then a new cycle starts In such instances, the P-R interval may reach unusually high values (0 56 sec in a personal case) High vagal tone is one of the causes of this disturbance, but a lesion of the conducting tissues should be postulated. If *a permanent or complete AV* block occurs, the prognosis becomes severe (Joly).

Episodes of *atrial flutter* or *supraventricular tachycardia* are rather common At times, *ventricular extrasystoles* (Fig 7-9A) or *ventricular escapes* may be seen, the latter are caused by hyperexcitation of the AV node, if they appear in the course of a severe pancarditis, they may favor heart failure (Kirby, 1948).

A change in the pattern of QRS (intraven-

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Roentgenology in rheumatic fever and rheumatic heart disease

JOHN B. SCHWEDEL

Roentgenologic techniques and their general relationship to the individual cardiac entities have been discussed in previous chapters.[1] Here an attempt will be made to correlate the data supplied by these techniques with the clinical findings of states currently associated with rheumatic heart disease. The information which may be derived may tend to confirm or disprove the etiologic diagnosis, may at times indicate the age of onset of carditis and the relative duration of combined lesions, may determine some of the roentgenologic manifestations of an active rheumatic carditis (rheumatic activity), or may explain some of the signs and symptoms associated with rheumatic heart disease.

GENERAL CONSIDERATIONS

Rheumatic carditis affects the pericardium, myocardium, and endocardium, not all of them in equal degree, nor all at the same time.

In the stage of fibrinous or early serofibrinous *pericarditis*, there are no evident roentgenologic manifestations. These appear only if the serous or serosanguinous effusions are great enough to distend the sac, thus modifying the usual cardiac silhouette or interfering with cardiac function. *Myocarditis* manifests itself by chamber enlargement. *Endocarditis*, involving, as it does, the valves, adds to the degree of chamber enlargement associated with the *myocarditis*.

[1] See Part 3, Chap. 8. *Editor*

In the *healing or healed stages* of rheumatic heart disease, the most conspicuous roentgenologic manifestations are those of *cardiac enlargement*, involving one or more of the heart chambers. Manifestations of healed pericarditis are extremely rare. Direct visualization of scarred valves is not possible until secondary calcification occurs. Such calcification rarely occurs early in the course of valvular deformity, but in the late teens and in adult life it is often found, when looked for specifically.

The most frequent site of valvular deformity is the *mitral valve*, resulting in stenosis, insufficiency, or both. The next most frequent valve involved singly is the *aortic*, resulting in stenosis, insufficiency, or both. However, the combination of mitral and aortic valvular deformity is common enough to warrant attempts to assay the role that each plays in the resulting multiple-chamber enlargement. Deformity of the *tricuspid valve* is rather common. However, it is often difficult if not impossible to determine if the consequence of chamber enlargements is due to deformity of this valve or to its functional incompetence. Deformity of the *pulmonary valve* is not common, and the degree of such involvement is rarely great enough to affect the right ventricle dynamically (pulmonary insufficiency) or to obstruct the flow of blood into the pulmonary artery (acquired pulmonary stenosis).

In consequence of the above considerations, it is possible to presume that certain combina-

present, the electrocardiographic alterations allow one to estimate the severity of the hemodynamic alteration and chiefly the occurrence of pulmonary hypertension.

The electrocardiographic signs due to the valvular stenosis consist of alterations in the duration, amplitude, morphology, and axis of the *P wave* due to dilatation and hypertrophy of the left atrium, and proportional to it. These signs are far from being pathognomonic because a "mitral P wave" can be found in other conditions, including constrictive pericarditis (Soulié, 1950). Prolonged duration of the P wave of more than 0.10 sec is seen in over 50 per cent of the cases (Carouso, 1950); it may be even longer than 0.12 sec The P wave appears in a form of a notched double-peaked plateau in leads I and II; this typical pattern is present in more than two-thirds of the cases (Carouso, 1950) (Fig. 7-10). In the right precordial leads, the P wave assumes a diphasic form (plus-minus type), with a small positive wave followed by a deep and broad negative wave; this is characteristic of *left atrial hypertrophy* (Fig. 7-10A) On the other hand, a diphasic P wave with two waves of the same voltage (or with the first, positive, wave higher than the second, negative wave) indicates *right atrial hypertrophy* (Carouso, 1950). The broad, notched, and diphasic P wave is explained by prolongation of the normal electrical asynchronism between activation of the two atria On the other hand, tracings taken directly on the external surface of the atria show that, in mitral stenosis, the left atrial tracing has a higher voltage than normal (Reynolds, 1953). However, the increased potential of the P wave in lead I may not be related to the size of the left atrium (Soulié, 1950).

The electrical axis of the P wave is slightly deviated *to the left*, the âP being in the neighborhood of 45° (Carouso). A marked deviation to the left becomes evident in cases of associated aortic insufficiency, while a deviation to the right occurs in cases with associated pulmonary lesions or tricuspid insufficiency (Soulié, 1950). An increased voltage of the P wave in leads II and III (*P pulmonale*) seems to parallel increased pulmonary artery pressure. The changes of P which appear when right ventricular systolic pressures are above 40 mm Hg (Gibert-Queralto, 1955) may be significant if the QRS complex is still within normal limits or shows a slight deviation toward the right (Cosby, 1953).

Atrial fibrillation is so frequent in mitral stenosis that the presence of this arrhythmia plus right axis deviation (or a vertical axis) is suggestive of this valvular lesion. The other common cause of atrial fibrillation, i.e., myocardial sclerosis, is usually associated with left axis deviation. Atrial fibrillation is more frequent when the left atrium is severely dilated, as in the association with mitral insufficiency. *Atrial flutter* and *atrial extrasystoles* are also frequent in mitral stenosis.

Even though mitral stenosis is often accompanied by disturbances of atrial excitability and of intraatrial conduction, it is unusual to find an important delay in AV conduction: the P-R interval is only rarely greater than 0.20 sec. On the other hand, rare cases of AV block have been reported (Di Matteo, 1949).

The alterations of the QRS complex are due to *systolic overload of the right ventricle* caused, first, by the "mitral block" and, later, by an additional obstruction at the level of the pulmonary arterioles (Fig. 7-10D). The right ventricular overload may be associated with a left overload if significant mitral insufficiency is also present.

It has been stated that no significant changes in the QRS complex occur if right ventricular pressure is below 60 mm Hg at rest (Gibert-Queralto, 1955). Occasional normal ECGs have even been reported in cases with intraventricular pressures higher than 60 mm Hg (Cosby, 1953). Evidence of right ventricular hypertrophy is usually present when the total pulmonary resistances are above 1,000 dynes/cm^{-5}/sec in pure mitral stenosis, but it may be absent in cases with associated mitral or aortic insufficiency (Scott, 1955) Finally, patients with a mitral area lower than 1 2 cm^2 may present normal tracings as far as the QRS complex is concerned (Scott, 1955). Thus, it follows that, in cases with left atrial pressure so elevated as to cause exertional dyspnea, the ECG may show no evidence of right ventricular overload whenever the arteriolar pulmonary resistance is not significantly increased. It seems that the resistances must be increased at least four times to cause a constant pattern of right ventricular hypertrophy (Joly, 1953).

The earliest sign of *right ventricular hypertrophy* is represented by a deviation of the axis *to the right* (Fig. 7-10D) associated with

to increased resistances to flow in the lungs or at the mitral valve.

Dilatation of the Superior Vena Cava. This structure, when distended, may be noted as a vertical right paravertebral density extending to the apex of the lung. Such dilatation occurs with pericardial effusions and with right-sided failure, regression in the vena caval distention corresponds to a fall in central and peripheral venous pressures.

Hilar Branches of the Pulmonary Artery. These branches dilate with acute or subacute increases in pulmonary arterial pressure, subsequently declining to their original state, or close to it. The pulmonary artery trunk, too, dilates, but its prominence is compounded by such factors as the height of the diaphragm, the respiratory phase, the heart shape, and the variations in width, even of the normal pulmonary artery so as to make such evidence somewhat less than reliable. The primary branches (right and left) of the pulmonary artery are difficult to visualize, except by angiocardiography. Of the two secondary (hilar) stems, the left is often hidden within the heart density. This leaves the right hilar stem with its branches, and particularly the descending portion, which generally is available for close inspection and measurement. Such inspection is facilitated by the interposition of the right bronchus separating the pulmonary artery branch from the right cardiac contour or density.

An increase in measurable width from the normal 9 to 14 mm (in the teleoroentgenogram) indicates evident distention. When increased width is present, pulmonary hypertension exists (in rheumatic heart disease, but not in congenital heart disease where increased flow may distend the pulmonary artery). However, absence of dilatation does not rule out pulmonary hypertension. To determine the presence or degree of pulmonary hypertension, cardiac catheterization is necessary.

Acute or subacute progressive and regressive changes occur with rheumatic carditis affecting the left side of the heart, but also with lung involvement, as in pulmonary hypertension secondary to hypoxia, pulmonary or bronchiolar inflammation, and pulmonary embolism. The differentation between these and the changes associated with rheumatic carditis obviously will have to be made on a clinical basis.

Pulmonary Vascular Changes. In the course of active carditis, especially when the left atrium is overdistended, the usual air-to-parenchyma ratio is likely to be disturbed by an increase in width and tortuosity in the minute vessels (venules, capillaries), increased pulmonary vascular content, and transudation of fluid into alveoli. The resultant picture is that of diffuse or mottled clouding and, if severe, large conglomerate areas of density accompanied by the clinical manifestations, either of pulmonary edema or its lesser counterpart, paroxysmal dyspnea. The two latter conditions are likely to be accompanied by manifestations of increased pulmonary artery width.

MITRAL STENOSIS

This type of obstruction to flow of blood from the left atrium into the left ventricle is characteristically associated with *left atrial enlargement* and a *normal or diminished size of the left ventricle.* The diagnostic feature is the relative disproportion in size of the two chambers rather than the grade of left atrial enlargement, since the left atrium can also be enlarged with various types of left ventricular failure. *Enlargement of the right ventricle* frequently occurs secondary to the increased mitral valvular obstruction and to increased pulmonary arterial resistance. The right ventricular hypertrophy consequent to this increased load is responsible for the rotation of the heart on its vertical axis. Consequently, there is straightening of the left upper cardiac contour in the PA view, diminution in the size of the aortic knob (or even its total disappearance), and rotation of the normal or small-sized left ventricle posteriorly. At the same time, the posteriorly placed left atrium, now enlarged, appears on the right cardiac contour as *a double contour,* and its density, superimposed on that of the right atrium, is increased, causing a double density. The *left auricle is also enlarged* and often is seen above the left ventricular contour in the PA view as an independent bulge (Fig 7-12A). These alterations in the cardiac contour are frequently described as *mitral configuration,* but the use of this term is misleading in that other conditions such as pulmonary heart disease or congenital shunts may result in rotation,

an increased voltage of the P wave. Marked right axis deviation is rare, and usually the axis is vertical. In the precordial leads, alterations of the ventricular complex appear later, and even for high ventricular pressures, they never show patterns similar to those encountered in pulmonic stenosis. Indeed the R/S = 1 is in itself quite an important index of right ventricular hypertension, whereas absence of S in lead V1 speaks for pulmonary hypertension higher than 100 mm Hg (Chavez, 1955). *Disturbances of right intraventricular conduction* are suggestive of right ventricular hypertension (Fraser, 1955), even though right BBB is rare. It should be kept in mind that intraventricular conduction defects may be related to myocardial lesions of rheumatic origin and thus may have no connection with hemodynamic abnormalities

Evidence of associated *left ventricular overload* are encountered in cases with associated mitral or aortic insufficiency

In summary, alterations of the P wave suggestive of left atrial dilatation are frequently present in pure mitral stenosis. Evidence of right ventricular overload and a markedly elevated voltage of the P wave reveal the existence of a high pressure gradient in the pulmonary circulation between pulmonary artery and pulmonary capillaries Thus, the absence of signs of right overload does not exclude the possibility of severe pulmonary capillary hypertension. This is why, in some patients, the ECG does not reflect the degree of mitral block.

Electrocardiographic alterations after exertion (depression of S-T) may occur. They reveal a relative coronary insufficiency due to low cardiac output (Vonk, 1956).

During *cardiac catheterization*, the ECG may show various arrhythmias and conduction disturbances which are not related to the valvular lesion.

Mitral commissurotomy is usually followed by some modifications of the ECG. During surgery, when the finger is forced through the mitral valve, short paroxysms of *ventricular tachycardia* are frequent, depression of S-T, intraventricular conduction disturbances, and shifting pacemaker may be observed (Campbell, 1952). A few hours or days after surgery, paroxysms of *atrial flutter* or *fibrillation* may occur Depressed S-T and negative T waves are often observed in the first postoperative week. These changes, which are due to subepicardial lesions and pericarditis, usually disappear within a few days (Puddu, 1952). Usually the P-R interval is not affected, if prolonged, it indicates possible recurrence of rheumatic carditis.

Permanent changes usually occur a few months after surgery. While modifications of the P wave are seen earlier, QRS usually becomes normal in 5 to 12 months (Joly, 1953). The P wave does not change its shape or duration but becomes lower if it was tall (Janton, 1956) and may cease to be diphasic in the right chest leads. However, alterations of the P seem to persist in more than one-half the cases, even when clinical and hemodynamic conditions are definitely improved. On the other hand, the modifications of the ventricular complex proceed parallel to the hemodynamic improvement. Therefore, the ECG plays a definite role in the postoperative evaluation of the patients. Regression of the patterns of right ventricular hypertrophy may require more than 3 years but then may be complete (Soulié, 1952). The regression of the pattern of right ventricular overload, besides the diminution of the R waves in right precordial leads and of the S wave in left precordial leads, includes a shift of the axis of QRS to the left The appearance of signs of marked left ventricular overload after commissurotomy is definite evidence that a significant mitral insufficiency has appeared, even in the absence of an apical systolic murmur.

In conclusion, the decrease or disappearance of signs of right ventricular overload after surgery confirms the improvement; on the contrary, their persistence casts doubts as to the actual improvement.

MITRAL INSUFFICIENCY

Pure mitral insufficiency is rare. It causes an *overload of the left ventricle*, and through an elevation of the pulmonary capillary pressure, it may cause also an overload of the right There is marked dilatation of the left atrium, yet the P wave frequently is not broadened and is notched in only one-half of the cases (Berliner, 1938).

Extrasystoles are common; they are more often ventricular in contrast to those observed in mitral stenosis (Brigden, 1953). *Atrial fi-*

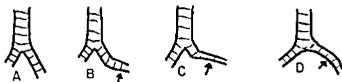


Fig 7-14. The bronchi in mitral valvular disease. LAO position A Normal. B. Elevation of the distal portion of the left bronchus C. Elevation and compression of the left bronchus D. Central elevation and compression of both bronchi by left atrial enlargement. Compression can occur only while bronchial cartilage is still pliable

ment is best noted during inspiration, even though inspiration itself is often accompanied by lordosis and an oblique esophageal course.

In the LAO position, the *space below the left bronchus is filled in* by either the atrium or the associated distended pulmonary veins, or both Later, there is actual *upward displacement of the left main bronchus.* Evaluation of upward displacement of the left main bronchus is not so important as is the demonstration of the left atrial backward bulge in the RAO position, since the latter usually occurs long before the bronchus is elevated (Fig 7-14).

Calcification of the mitral valve should be sought for by coming down (narrowing) of the shutter aperture and is best seen in the RAO position, less frequently in the PA or LAO position Various grades of linear calcifications may be discerned, with vertical and rotary motion having a magnitude of at least several millimeters downward in systole, upward in diastole Mitral valvular calcification can be observed in 50 to 75 per cent of patients with mitral stenosis Location of such a calcified valve also may be used as an aid in the quantitative evaluation of the degree of enlargement of the left atrium, since here one may estimate left atrial depth extending from the mitral valve to the posterior left atrial contour

MITRAL INSUFFICIENCY

With mitral valvular deformity, at times it is difficult to determine which predominates, stenosis or insufficiency. However, for the purposes of this discussion an attempt will be made to determine only if insufficiency is present rather than its relative degree.

Numerous clinical findings such as a long, loud systolic apical murmur transmitted to the axilla, partially or wholly replacing the 1st sound, absence of the opening snap, or demonstrable left ventricular enlargement suggest that mitral valvular insufficiency may be significant. Electrocardiographic findings of left ventricular enlargement or hypertrophy also suggest that mitral insufficiency is present, though concomitant aortic valvular deformity might also cause such left ventricular enlargement to be seen on the ECG or roentgenogram.

Pulmonary artery wedge pressures or data obtained by transthoracic or transbronchial catheterization, where direct left atrial pulse and pressure curves may be inscribed, are often difficult to assess. An early rise following the C wave, a wave larger and higher than the C wave, and a precipitous fall off of the descending limb of the V wave are all

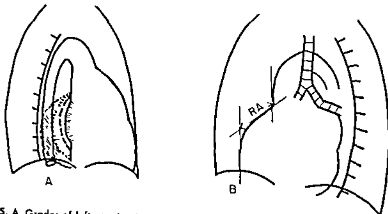


Fig. 7-15. A. Grades of left atrial enlargement RAO position Slight (+), moderate (++), marked (+++), excessive (++++) B Right atrial enlargement.

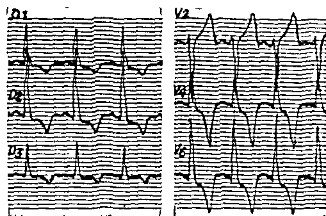


Fig. 7-11. Aortic valvular stenosis in a 19-year-old patient of slender build. The ECG shows a systolic overload of the left ventricle with high voltage of R and alteration of repolarization in V_6. Concordant inversion of the T wave in the standard leads.

overload of the left ventricle (Cabrera, 1952). This, however, is an inconstant finding, even in patients with no coronary lesions. The delay of intrinsicoid deflection in V_5 or V_6 associated with a left axis deviation is suggestive of an aortic lesion (Cabrera, 1949), while the presence of *left BBB* is more in favor of syphilitic aortitis (Friedland, 1949)

Finally, rheumatic aortic insufficiency may show alterations of the P wave (Friedland, 1949) or atrial fibrillation more frequently than syphilitic regurgitation.

TRICUSPID INSUFFICIENCY

Tricuspid insufficiency is characterized by overloading of both the right atrium and the right ventricle.

Atrial enlargement is revealed by greater voltage of the P wave and marked deviation to the right of its axis. *Right ventricular overload* is shown by a delay of the intrinsicoid deflection in leads V_1 and V_2 (Aceves, 1947). This delay is often remarkable (>0 06 sec) but is evidence of a tricuspid lesion only if there is atrial fibrillation or evidence of right atrial dilatation (Cabrera, 1949). The presence of a small Q wave in lead I associated with a right axis deviation of QRS is likewise suggestive of a tricuspid lesion. The delayed intrinsicoid deflection in lead V_1 is often associated with a low voltage of QRS in the same lead (Sepulvedo, 1955). *The P wave is tall and diphasic (plus-minus) in the right precordial leads* and resembles the tall P waves of the esophageal leads.

When a mitral lesion is associated to the *tricuspid lesion, the P wave* becomes broad and notched (Smith, 1942). The ventricular overload becomes more manifest in these cases and is revealed by a predominant voltage of R lead in V_1

TRICUSPID STENOSIS

While pure tricuspid stenosis is rare, it is a rather frequent defect when associated with mitral stenosis and tricuspid insufficiency. In these cases, the axis of QRS is often deviated *to the right* (Smith, 1942).

Isolated tricuspid stenosis shows a *right atrial overload* characterized by high voltage *of P in leads II and III* (Friedlander, 1938). The P wave may be diphasic in the right precordial leads (Ellis, 1946).

Various arrhythmias have been observed: nodal tachycardia, AV dissociation, and nodal escapes (Friedlander, 1938).

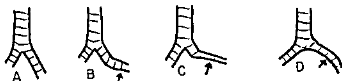


Fig 7-14. The bronchi in mitral valvular disease. LAO position. A. Normal B. Elevation of the distal portion of the left bronchus C Elevation and compression of the left bronchus. D. Central elevation and compression of both bronchi by left atrial enlargement. Compression can occur only while bronchial cartilage is still pliable.

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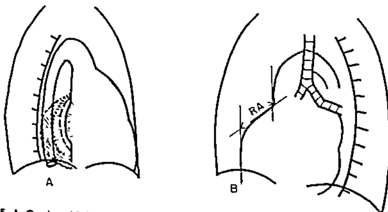


Fig 7-15. A Grades of left atrial enlargement RAO position. Slight (+), moderate (++), marked (+++), excessive (++++) B Right atrial enlargement

tions of chamber enlargements are common in rheumatic heart disease and are uncommon or less often noted in other disorders. Accessory data such as pulsations and valvular calcifications are confirmatory, but even in the absence of such confirmatory data, a proper inference may be drawn.

The diagnostic feature of the more characteristic disorders included in the term "rheumatic heart disease" will be described below, along with some of the more common variants.

MANIFESTATIONS OF RHEUMATIC ACTIVITY

The roentgenologic manifestations of rheumatic activity are based chiefly on:

1. Demonstration of the changes associated with pericardial effusion
2. Progression and regression in the size of individual heart chambers
3. Changes involving the superior vena cava
4. Manifestations involving the hilar branches of the pulmonary artery
5. Changes in pulmonary vascularity

Pericardial Effusion. This manifestation is fairly commonly recognizable in the course of active rheumatic carditis Slight grades of fluid accumulation, amounting to 150 ml in children, and perhaps to 250 ml in adults, are difficult to recognize in any single roentgenogram, but may be more readily evident when serial films are available for comparison Larger effusions occasionally may cause a characteristic *water-bottle contour,* but this must be differentiated from a diffuse multiple-chamber enlargement

Usually the course of pericarditis runs a period of 6 weeks or so, though slighter grades may run their course in several weeks and others (unusual) may persist up to 4 or 6 months.

Fluoroscopy is valuable in the recognition of the slighter grades of effusion. The amplitude of cardiac pulsations in the lateral contours may be normal or diminished, but are rarely so typical as to differentiate them from the variations in the normal or from those in hearts with greatly dilated chambers (Fig. 7-17).

However, it still is possible to utilize the presence or absence of pulsations in pericardial effusion. Since such effusions tend to gravitate to the lowest portion of the pericardial sac, which in the upright position means the inferior or noncontour-forming surfaces, it is possible to visualize such contours by existent or artificial means. Filling of the stomach bubble with air by means of carbonated beverages or by a Seidlitz powder permits the visualization of the inferior cardiac contours. At other times, the gas bubble in the stomach or an accumulation of gas in the distal transverse colon or splenic flexure may be adequate to serve the same end. The observed *absence of upward systolic pulsations* in the inferior contours is due to the collection of fluid in the dependent portion of the pericardial sac, particularly when contrasted to the normal, or perhaps slightly diminished pulsations, of the mid- and upper lateral contours, where fluid accumulation is less abundant.

Absent or greatly diminished pulsations of the lateral contour suggest more massive degrees of fluid accumulation, but only when marked or excessive cardiac enlargement (dilatation) can be ruled out by serial comparison films or by the clinical course of the disease Even in the presence of such marked degrees of enlargement, where pulsations may be of slight amplitude, there should be no disproportionate degree of damping of the amplitude of pulsations of the inferior cardiac contours.

Changes in Size of Individual Heart Chambers. In the course of active rheumatic carditis, various cardiac chambers may become enlarged In the absence of previous endocardial (in particular, valvular) involvement, all chambers may participate in such enlargement more or less to the same degree. However, when rheumatic carditis is associated with previous valvular involvement, the chamber(s) behind the damaged valve become enlarged. With cessation of rheumatic activity, regression in size occurs, usually only partial in degree, but at times apparently to the previous state The chambers most frequently involved in enlargement and regression are the left atrium and the left ventricle, in this order of frequency. Right ventricular and right atrial enlargement are less frequently encountered as the sole manifestation of active carditis, and even then, it is difficult to determine if the effect is due to inflammation, or is a consequence of left-sided failure, or is secondary

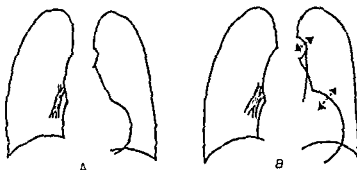


Fig. 7-16. A. Aortic stenosis. Concentric hypertrophy denoted by rounding of the upper left ventricular contour. B Aortic insufficiency. Left ventricular enlargement; aortic dilatation; increased amplitude of pulsations denoted by the double-pointed arrows.

cardiographically, or roentgenologically Laboratory methods make it possible to evaluate the extent of insufficiency by determining the presence and the degree of dilution of dye in the left atrium which had been selectively injected into the left ventricle These, when *computed along with simultaneously taken* cardiac outputs, offer relative quantitative retrograde flow values A more spectacular, but less valuable, variant is the injection of an opacified substance such as Diodrast into the left ventricle and noting if there is increased opacification of the left atrium Both of these methods have been attempted only rarely and so far have not been particularly conclusive except when the magnitude of regurgitation has been great

AORTIC STENOSIS

Aortic stenosis on a rheumatic basis is not common in young individuals, but with increasing age, patients with seemingly inconspicuous aortic systolic murmurs develop partial or typical forms, associated with faint or absent 2d aortic sounds, systolic thrill, and loud low-pitched murmurs transmitted into the neck, lowered pulse pressures and slowed heart rates, accompanied by precordial pain, dizziness, syncope, and rarely by convulsions The ECG shows left ventricular hypertrophy or systolic overload patterns

The roentgenologic manifestations of significant aortic stenosis in order of frequency are: *increased rounding of the left ventricular contour* without evident enlargement (concentric hypertrophy), slight to moderate grades of left ventricular enlargement (Fig. 7-16A). When aortic stenosis is associated with greater degrees of enlargement, another associated cause should be looked for, such as aortic insufficiency (at times, without striking pulse pressure increase or without clearly evident diastolic murmur). Mitral valvular insufficiency and, occasionally, unsuspected healed myocardial infarction might also be responsible for such added enlargement.

The ascending aorta may or may not be

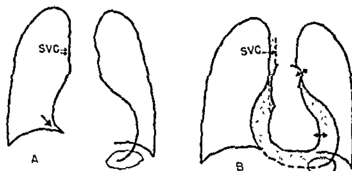


Fig. 7-17. A. Pericardial effusion Increased heart size where the right cardiophrenic angle is diminished (arrow), superior vena cava distended (double arrow); lower contour pulsations either absent or greatly diminished in amplitude. B. Diagram of (A) showing how aortic and left ventricular pulsations, usually already diminished, are greatly dampened because of the dependent accumulation of fluid.

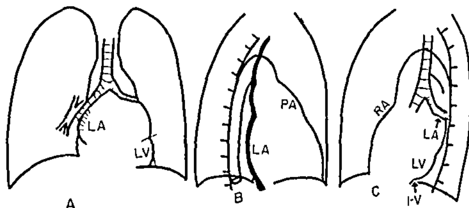


Fig. 7-12. A. Mitral stenosis. PA view. Left ventricle small. Left atrium large, appearing on the right as a double contour, its increased density also termed "double density." The aortic knob is small, the pulmonary artery (trunk) prominent, and the left atrial prominence is noted above the left ventricle. B. RAO position. Below the ascending aorta the contour of the pulmonary artery is prominent, owing in part to its dilatation, and also to enlargement of the right ventricle in its vertical length, displacing the pulmonary artery segment upward and forward. The barium-filled esophagus is indented from above first by the aortic arch, then by the right main branch of the pulmonary artery and its accompanying right main bronchus; the lowermost displacement is that due to left atrial enlargement. C. LAO position. The right atrial segment is not elongated. The left atrium is enlarged sufficiently to elevate the distal portion of the left bronchus. The left ventricular segment (indicating left ventricular depth) is not enlarged. Arrow points to interventricular groove.

and it is—to say the least—confusing to have this term applied erroneously.

The left atrium may be *not at all* enlarged in mitral stenosis, though this is unusual, or the left atrium may be slightly, moderately, or even markedly enlarged. The bulge of the left atrium posteriorly may be slight enough to indent the anterior surface of the barium-filled esophagus, while, later in the course of the disease, the esophagus may be displaced posteriorly. While, characteristically, the left atrium lies in the mid-portion of the retrocardiac space in the RAO position, it may be located lower down, overlying the diaphragm in horizontally shaped hearts, or where the heart has been displaced forward with the apex tilted upward. Thus, the characteristic feature of left atrial esophageal displacement is its effect on the barium-filled esophagus, irrespective of whether this occurs in the mid- or lower portions of the retrocardiac space. Tilting of the patient's chest forward is frequently helpful in discerning the slighter grades of left atrial enlargement posteriorly since such displacement is better noted optically from a vertical esophageal course than when the course of the esophagus is somewhat more oblique Optimal esophageal displace-

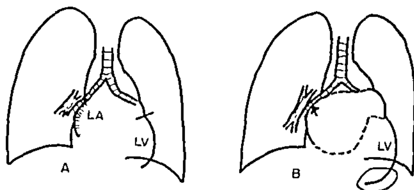


Fig. 7-13. A Mitral insufficiency. Left atrium and left ventricle are enlarged. B. A further example of advanced mitral insufficiency in that there is a greater degree of left ventricular enlargement; left atrial enlargement with expansile left atrial pulsations (arrow) displacing the right bronchus and the secondary (hilar) branch of the pulmonary artery outward and upward during left ventricular systole.

degrees of the patient's rotation into the LAO position Increasing *degrees of right atrial enlargement* are manifested *by further lengthening* of this segment lying between the *aorta* and the vertical portion of the *right atrium*. This segment becomes *more horizontal* and, *in extreme cases*, may even present a convex contour superiorly. At such times, even the intervenous portion of the *right atrium* may be demonstrably *enlarged and bulge posteriorly* above the diaphragm in the RAO *portion*, but to the right of a barium-filled esophagus and seemingly transected by the esophagus in the RAO position

Right ventricular enlargement occurs at the same time, or even precedes right atrial enlargement *Tricuspid valvular calcification occurs rarely*

TRICUSPID STENOSIS

Disproportionate right atrial enlargement in relation to a lesser grade of right ventricular enlargement might suggest an obstruction between these two chambers. This occurs in congenital tricuspid stenosis, but as far as the author knows, has *never been noted in* acquired tricuspid stenosis A delay in right atrial emptying might be demonstrable on angiocardiography

PULMONIC VALVULAR INVOLVEMENT

Slight or moderate deformities of this valve leading to insufficiency are not uncommon These are rarely of such degree as to impose a significant load on right ventricular function, certainly much less so than the increased resistance to flow in the lungs distal to the valve. Even more often the ultimate cause for the Graham Steell murmur noted during life is found *to* be due to dilatation of the annulus. *Frequently, too*, there is no valvular deformity or dilatation of the annulus to explain the *murmur, even* when the aortic valve is perfectly competent.

On fluoroscopy, the pulmonary artery trunk is noted to be dilated, in the RAO position, it *is prominent and bulges anteriorly. Its pulsations* are of normal or *increased amplitude* *An increased* amplitude of pulsation noted to extend to the secondary (hilar) branches, associated with *their widening*, and marked changes in density with systole and diastole is termed *hilar dance*, and generally is due to increased pulmonary arterial pulse pressures, analogous to the peripheral phenomenon, typical of aortic insufficiency.

Pulmonic stenosis on an acquired rheumatic basis occurs rarely and may be suspected only by the magnitude of the systolic murmur and thrill in the pulmonic area and by the *greatly dilated pulmonary artery trunk* seen on fluoroscopy or in the roentgenogram. Continued opacification of the pulmonary artery trunk on angiocardiography may be confirmatory; on rapid serial films, a thickened deformed pulmonary valve may be demonstrable

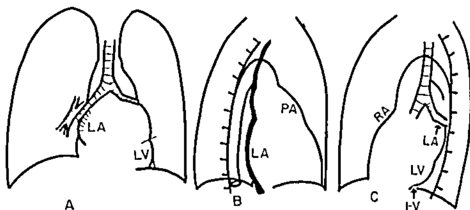


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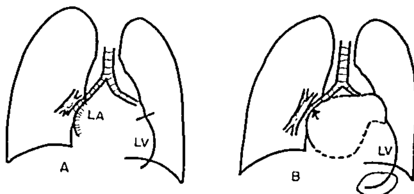


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stenosis). The splitting of the 2d sound is due to increased pulmonic pressure, causing prolonged right ventricular ejection and delayed closure of the pulmonic valve. The triple rhythm is related to tachycardia and higher pressure in the left atrium.

In later stages of the disease, some or all of these data may become permanent because of the establishment of an organic valvular lesion. However, usually the pulmonic murmur decreases in intensity.

It is important to differentiate the above signs from those heard in normal children

1. *A triple rhythm can be found in normal children* In the experience of the author, the 3d sound of a normal child is never larger than one-half of the 2d sound An exception may be represented by excitable subjects with extreme tachycardia Usually, reassurance and repeated testing lead to normalization of the heart.

2 One out of five presumably normal children present an *innocent systolic murmur* The murmur has been so termed because, in the great majority, the children develop normally and have no sequelae An alternative interpretation, involving a new concept of rheumatic fever, has been advocated by Luisada et al (1958) As this concept would not change the basic fact that most of these murmurs do not warrant a different name, no further reference to such a concept needs to be made here It is likely that various phenomena are grouped under this label, possibly including mild forms of congenital and rheumatic heart diseases Different types of murmurs have been described by Harris et al, comprising a "vibratory" and a "musical" murmur Graphic characteristics which should enable the observer to differentiate these innocent murmurs from those of acute rheumatic fever have been described by Harris et al, and by Wells (1956) *It is the opinion of the authors that no graphic differentiation is possible as yet.*

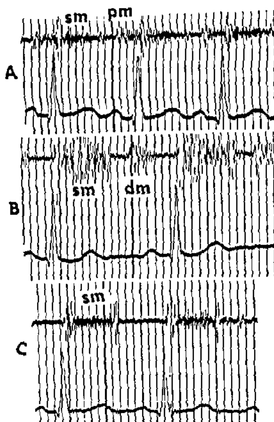


Fig. 7-20 Adolescent with acute carditis in three stages of evolution A. Systolic and presystolic murmurs at apex B Three months later; large systolic and diastolic murmurs. C. Six months later; soft, all systolic murmur.

Remarkable changes can be observed in the loudness, duration, and pitch of *musical* and *vibratory* murmurs during the course of rheumatic fever. Then, rheumatic fever either caused these murmurs or (if the children had them prior to the onset of the disease) modified their characteristics. Dismissal of these murmurs *only* because they are *musical*, *vibratory*, or *short* would be detrimental

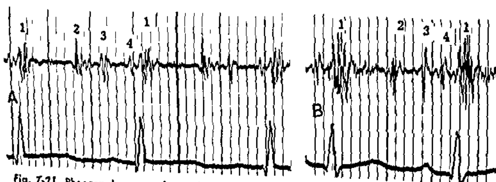


Fig. 7-21. Phonocardiograms of two children with acute rheumatic fever. Quadruple rhythm due to large 3d and 4th sounds

suggestive of mitral insufficiency, but not necessarily diagnostic. Combined left atrial and left ventricular pressures through the transthoracic or transbronchial routes simultaneously performed might indicate a *systolic left atrial gradient*, the direction of which is abnormal. Obviously, all these data, laboriously acquired, at times are not adequate to offer a definitive answer as to whether significant insufficiency is or is not present.

Roentgenologic aids are only accessory and bear no greater significance than the above-named diagnostic data, but when combined with other positive findings, the added data offer either a definitive clinical answer or a reasonable basis upon which clinical conclusions may be drawn. Such roentgenologic data in order of importance are:

1 Left ventricular enlargement

2. Left atrial expansile pulsations (Fig. 7-13)

The grade of *left ventricular enlargement* in mitral insufficiency uncomplicated by other lesions is generally only slight to moderate. This generally can be recognized by noting the increased length of the left ventricular contour, usually best seen in the PA position, by either downward elongation or rounding, and later on by increase in depth of this chamber, best noted in the LAO position

Left atrial enlargement in mitral insufficiency may be slight, moderate, marked, or extreme. It has been stated that the most marked grades of left atrial enlargement occur in mitral insufficiency, and certainly this is often true However, it is also true that the grade of left atrial enlargement in uncomplicated mitral stenosis may be just as great. Thus, the grade of left atrial enlargement in these two conditions (mitral stenosis, mitral insufficiency) does not help in the differential diagnosis The characteristic criteria of left atrial enlargement have been described in a previous chapter [2] but, for the sake of continuity will be repeated here

Slight to moderate grades of left atrial enlargement generally are noted as a "bulge" posteriorly into the retrocardiac space, often compressing or displacing the barium-filled esophagus backward. The appearance of left atrial density to the right in the PA view, as well as the identification of an accessory bulge between the contours of the pulmonary artery and the left ventricle, and the demonstration of elevation or compression of the left main bronchus, or both, occur later in the course of enlargement of this chamber.

The demonstration of compression of the left main bronchus, however, is significant since such compression could have occurred only at a time when the bronchial cartilage was pliable and compressible, that is, up to the mid- or late teens. In early adult life, such compressibility is lost, and left atrial enlargement upward can only displace the bronchus, but not compress it.

The demonstration of *systolic expansile pulsations* is by far the most typical diagnostic feature in mitral insufficiency. The right main bronchus and the right descending branch of the pulmonary artery move laterally during systole, in a transmitted fashion.[3] This may be compared to the intrinsic expansion and narrowing of the pulmonary artery when the pulmonic pulse pressures are increased (intrinsic pulsations, hilar dance).

Mitral valvular calcification is frequently found to be associated with mitral insufficiency. However, it probably is not more frequent in mitral insufficiency than in mitral stenosis. At times, the increased length of such demonstrable mitral valvular calcification may suggest a large valve with insufficiency rather than stenosis. However, since diameters of mitral valvular annuli differ considerably from person to person, an error may be introduced when basing an assumption on such increase in length of demonstrable calcification (Fig. 7-18)

Right ventricular and right atrial enlargement in mitral insufficiency does not vary significantly from that noted in mitral stenosis but tends to be less In both, it is a consequence of the obstruction to pulmonary flow, with myocardial effects ending in right heart failure

As noted above, differentiation between predominant stenosis over insufficiency, or insufficiency over stenosis, is extremely difficult to assess All one can do is to help determine if enough insufficiency is present to cause some of its manifestations clinically, electro-

[2] See Part 3, Chap. 8. *Editor.*

[3] This expansive movement is clearly revealed by roentgen kymography, esophagocardiography, and electrokymography (Part 4, Chaps 8 and 10). *Editor.*

no diastolic gradient across the mitral valve and evidence of regurgitation, who presented this snap It should be *noted* that the vibration was *small* and not too high pitched, on the one hand, and, on the other, that moderate stenosis may exist without a gradient.

One of the diastolic sounds (3d sound, 4th sound, or both) may become unusually large (Figs. 7-22, 7-23, and 7-24). When only one of them is large, auscultation reveals a *triple rhythm*, when both are large, auscultation frequently gives the wrong impression of a diastolic rumble, leading to the incorrect diagnosis of mitral *stenosis* While this phenomenon is more common in children, it may be observed also in adults, particularly during active rheumatic carditis

Tracings recorded over the pulmonic area may reveal a different type of *systolic murmur having the shape of a diamond* This should be considered as due to "relative" pulmonic stenosis, i e., to eddies caused by dilatation of the pulmonary artery. Increased pressure of the pulmonary circulation is the obvious explanation. The 2d sound is frequently large but *seldom split* Splitting, with the louder (pulmonic) component following the aortic, is already evidence of severe pulmonary hypertension Then, mitral regurgitation is severe,

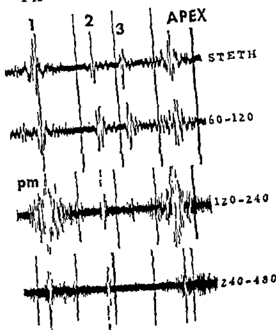


Fig. 7-24 Minimal mitral stenosis (6 months later, left heart catheterization revealed a mitral diastolic gradient of 2 mm) plus probable active carditis. Apical tracings in various bands There is triple rhythm (large 3d sound) and a presystolic murmur. A year later, the presystolic murmur had disappeared.

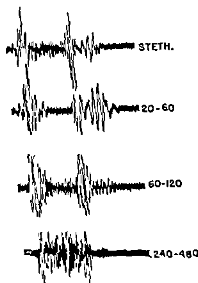


Fig. 7-23 Case of mitral insufficiency where the late systolic type of murmur is revealed by a "filtered" tracing in the 240 to 480 cps range

or there is an associated stenosis, or there is left ventricular failure.

Mitral Stenosis. Patients with narrowing of the mitral valve may have different auscultatory phenomena and may present various phonocardiographic findings.

1. *Closing snap of mitral valve.* The 1st sound is typically deformed. It starts with a series of 5 to 8 small vibrations of fairly high frequency and small amplitude, which last through the RS wave and somewhat later, then culminate in a rapid vibration of tremendous amplitude This is due to the noisy, sharp, and delayed closure of the mitral valve, or to a vibration replacing the closure, if there is a rigid funnel (Fig 7-26B)

2 *Prolonged and variable Q-1 interval.* The interval Q-1, measured from the beginning of Q to the onset of the first large vibration of the 1st sound, normally measures 0 04 to 0.07 sec The first large vibration may even coincide with the peak of R. In mitral stenosis, this interval is prolonged (Wells) and may measure 0 08 to 0 10 sec (Fig 7-25B). If there is arrhythmia caused by atrial fibrillation, this interval varies in length, being longer

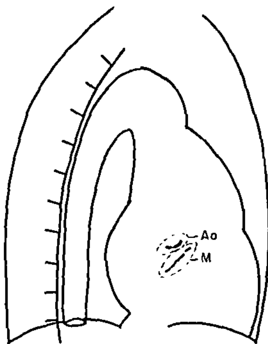


Fig. 7-18. Aortic and mitral valve calcification. Usually this is recognized most often in the RAO position as calcific densities within the mid-portion of the cardiac density, having characteristic up and down (aortic) or rotary (mitral) pulsations *Ao*, aortic, *M*, mitral.

dilated. If it is dilated, it is assumed that the dilatation is caused by the jet effect of high-velocity flow on the aortic wall. Such dilatation of the lateral or anterior walls is noted by *increased convexity or arching of the ascending aorta* in the PA and LAO positions However, if the jet flow is directed medially or posteriorly, the resultant dilatation is no longer evident by the usual roentgenologic techniques, though it may well be demonstrable with angiocardiography or aortography Not infrequently, there is no actual aortic dilatation, presumably because of decreased left ventricular output of long duration, imposed by the valvular narrowing

The *amplitude of aortic pulsations* may be increased, decreased, or normal and is not characteristic of this condition

Demonstrable *valvular calcification* is perhaps the most striking roentgenologic feature It can be demonstrated in about four out of every five patients who present themselves with other features of aortic stenosis Linear or semicircular densities, generally bearing a horizontal or semihorizontal position, move predominantly up and down with each cardiac cycle, though at times this motion is from high up posteriorly to down anteriorly for a distance of ½ to 1 cm. Aortic valve calcification is generally best noted in the RAO position within the mid-portion of the heart density, or slightly above (Fig. 7-18).

AORTIC VALVULAR INSUFFICIENCY

The second important variety of aortic valvular deformity is that of aortic insufficiency. Here there is a reflux of blood during diastole, increasing the left ventricular load Aortic insufficiency can be differentiated into two types, one with considerable, the other with relatively slight reflux With considerable reflux, the diastolic filling is great, ejection is rapid. The enhanced peripheral flow causes a characteristic aortic curve with high peaking and a low incisura on the descending limb. High pulse pressure and pistol-shot sounds are the clinical concomitants of such aortic curves The rapid and forceful ventricular ejection is associated with enhanced systolic distention of the aorta and also a sharp elastic recoil in diastole.

When there is a high pulse pressure, the left ventricle enlarges moderately, markedly, or excessively (Fig. 7-16B). Its pulsations, as well as those of the dilated aorta, are of increased amplitude.

The second type of aortic insufficiency is that not associated with increased pulse pressure Presumably the degree of reflux is slight, and there may be few or no roentgenologic manifestations—slight or no left ventricular enlargement, no enhanced aortic pulsations.

Valvular calcification may occur with either of the two types of aortic insufficiency outlined above However, if aortic stenosis is associated with the insufficiency, even if the aortic insufficiency is clinically predominant, valvular calcification is much more common than with aortic insufficiency alone

TRICUSPID INSUFFICIENCY

Both clinically and roentgenologically, it is impossible to differentiate between organic and functional tricuspid insufficiency. Neck vein distention, liver enlargement, and edema are common to both, increased amplitude of the A waves of the jugular tracing and prominent P waves and Rs pattern in the right precordial leads of the ECG are common to both

Demonstration of *right atrial enlargement* is a presumptive evidence for the diagnosis of tricuspid insufficiency This is best determined by observation of the *increased length of the right atrial (oblique) segment* in the early

no diastolic gradient across the mitral valve and evidence of regurgitation, who presented this snap. It should be noted that the vibration was small and not too high pitched, on the one hand, and, on the other, that moderate stenosis may exist without a gradient.

One of the diastolic sounds (3d sound, 4th sound, or both) may become unusually large (Figs 7-22, 7-23, and 7-24). When only one of them is large, auscultation reveals a *triple rhythm*, when both are large, auscultation frequently gives the wrong impression of a diastolic rumble, leading to the incorrect diagnosis of mitral stenosis. While this phenomenon is more common in children, it may be observed also in adults, particularly during active rheumatic carditis.

Tracings recorded over the pulmonic area may reveal a different type of *systolic murmur having the shape of a diamond.* This should be considered as due to "relative" pulmonic stenosis, i e, to eddies caused by dilatation of the pulmonary artery Increased pressure of the pulmonary circulation is the obvious explanation The 2d sound is frequently large but *seldom split* Splitting, with the louder (pulmonic) component following the aortic, is already evidence of severe pulmonary hypertension Then, mitral regurgitation is severe, or there is an associated stenosis, or there is left ventricular failure.

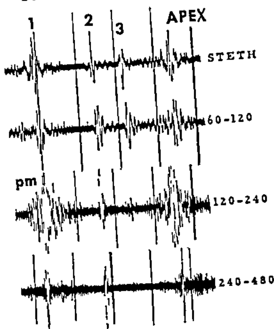


Fig. 7-24. Minimal mitral stenosis (6 months later, left heart catheterization revealed a mitral diastolic gradient of 2 mm) plus probable active carditis. Apical tracings in various bands There is triple rhythm (large 3d sound) and a presystolic murmur. A year later, the presystolic murmur had disappeared.

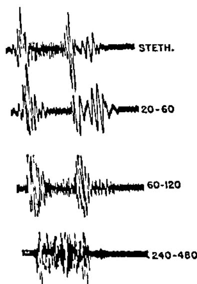


Fig 7-23 Case of mitral insufficiency where the late systolic type of murmur is revealed by a "filtered" tracing in the 240 to 480 cps range

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The phonocardiogram in rheumatic fever and rheumatic heart disease

ALDO A. LUISADA AND ARIO B. ZILLI

RHEUMATIC FEVER

The sound tracing of patients with acute rheumatic fever supplies data which are of help for confirmation or clarification of the auscultatory findings and, in certain cases, for establishing a correct diagnosis

The most common findings are

1. A prolonged 1st sound at the apex
2. A systolic murmur "in decrescendo" of high pitch (*soft murmur*) or a short murmur with regular vibrations (*musical or sea-gull type of murmur*) at the apex and midprecordium (Fig 7-19A).
3. A split 2d sound over the pulmonic area (Fig 7-19B).
4. A systolic murmur over the pulmonic area. This is usually "diamond-shaped" and of a lower pitch than the apical murmur (Fig. 7-19B).
5. An increased loudness of the 3d sound (more seldom of the 4th) at the apex, creating either a *triple rhythm* (gallop rhythm) (Taquini et al., 1940) or a *quadruple rhythm* (Fig. 7-21)
6. A short and low-pitched early diastolic rumble or, more seldom, a presystolic murmur, over the midprecordium (Figs. 7-20 and 7-24).

Any or all of these findings may be present (Luisada and Magri; Zilli and Gamna), and may disappear following recovery. Their evaluation is not always easy. The apical systolic murmur is probably caused by dilatation of the left ventricle and edema of the mitral valve and the papillary muscles ("relative" mitral regurgitation). A possible explanation for the "musical" murmur is vibration of an edematous papillary muscle. The diastolic or presystolic rumble is a functional phenomenon caused by dilatation of the left ventricle and increased diastolic pressure in the left cardiac chambers (relative mitral stenosis) The pulmonic systolic murmur is caused by dilatation of the pulmonary artery and the eddies which form in it ("relative" pulmonic

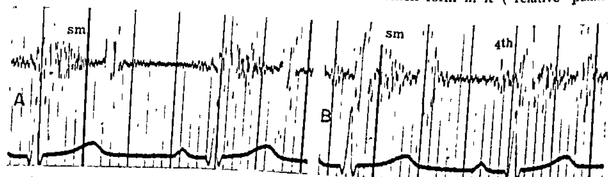


Fig. 7-19. Phonocardiograms of an adolescent with acute rheumatic carditis. A. Systolic murmur in decrescendo at apex. B. Diamond-shaped and larger systolic murmur over pulmonic area; split P_2; 4th sound.

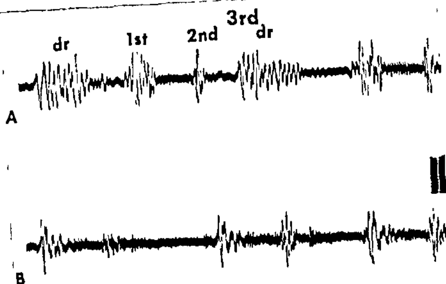
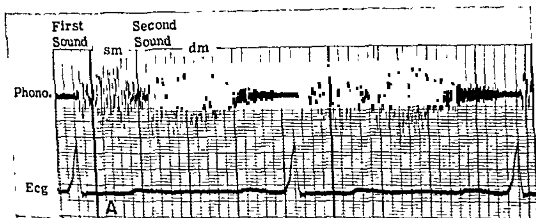


Fig. 7-27. "Relative" mitral stenosis in a case of coronary and hypertensive heart disease with aortic insufficiency. A Large diastolic mumble following a 3d sound during heart failure. B. Minimal diastolic vibrations after recovery



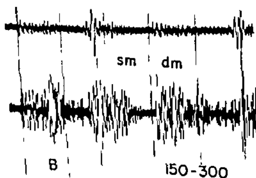


Fig. 7-28. A. Rheumatic heart disease Diamond-shaped systolic murmur (early diamond); large 2d sound; long diastolic murmur in crescendo-decrescendo. Phonocardiogram at aortic area. Severe aortic insufficiency, minimal aortic stenosis. B. Rheumatic heart disease. Systolic murmur in decrescendo and typical diastolic murmur in decrescendo at aortic area Severe aortic insufficiency, minimal aortic stenosis. Filtered tracing at the base

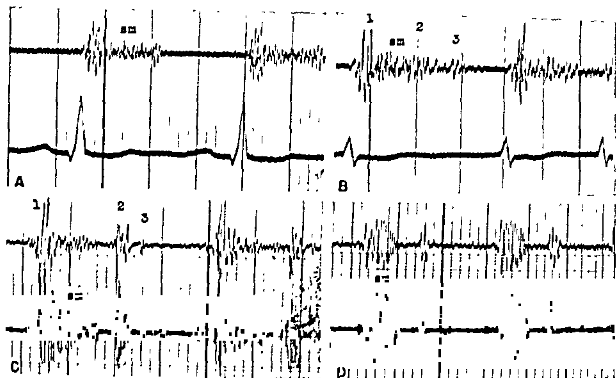


Fig. 7-22. Four cases of pure mitral insufficiency (catheterization of left heart). Phonocardiograms at apex reveal a long systolic murmur in decrescendo. (A) and (B) tracings are "stethoscopic" and have an ECG for timing. (C) and (D) tracings are "stethoscopic" phonocardiograms superimposed on filtered tracings (band 150 to 250). The latter emphasizes the type in decrescendo of the murmur.

in many cases of rheumatic fever On the other hand, the "crescendo" systolic apical murmur described by Wells should be considered evidence of mitral regurgitation, until proved otherwise

RHEUMATIC HEART DISEASE

Mitral Insufficiency. In initial or mild insufficiency, only a *prolongation* of the central phase of the 1st sound is present Later, the vibrations of the 1st sound continue during the first half of systole with decreasing intensity. When mitral insufficiency is established, three types of murmurs can be recorded.

1. A *systolic murmur* with gradually decreasing amplitude of vibration (*murmur in decrescendo*). This murmur has both high- and low-pitched vibrations, but the high predominate. It is a common finding, and probably indicates that the magnitude of regurgitation is not great. Selective phonocardiography usually records this murmur in the range 150 to 250 vibrations per second (Fig. 7-22C, D)

2 A *systolic murmur which continues throughout systole* with the same intensity The vibrations are mostly high pitched (soft murmur—range 200 to 400). This *all-systolic* or *holosystolic murmur* is less common and indicates a severe regurgitation (Fig. 7-22A, B).

3 A *late-systolic murmur in crescendo.* Actually the vibrations occupy all of systole but are greater in late systole before the 2d sound (Figs 7-23 and 7-29A) This murmur has been considered as the rule by Leatham but was not recorded too often by the authors. It is possible that this difference of opinion can be explained by different characteristics of the recording apparatus Records taken with filters in the frequency range 200 to 400 undoubtedly show more commonly a "crescendo" murmur Such a type of murmur is logical if one considers that *pure* mitral insufficiency has a wave of regurgitation (I wave in a pressure tracing of the left atrium) with a peak in late systole [1]

The first high vibration of the 1st sound may be large (*closing snap of the mitral valve*), but the Q–1st sound interval is normal and measures less than 0 08 sec, unless there is an associated stenosis (Wells).

An *opening snap of the mitral valve* may be visible This phenomenon has been accepted in the past as evidence of mitral stenosis. However, the authors studied a few cases, with

[1] See Chap. 13.

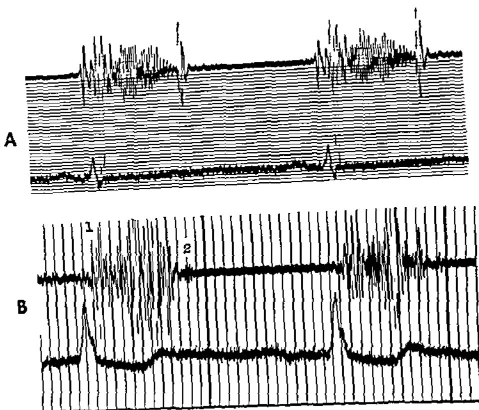


Fig. 7-30 Comparison between the murmur of relative aortic stenosis, early diamond, (A) and that of obstructive aortic stenosis, late diamond, (B) (From Aravanis and Luisada. Am. Heart J. 1957)

shorten the interval by promoting such opening, this prolongation is never excessive Mitral commissurotomy, by decreasing left atrial pressure, decreases this interval (Haring et al) This interval is typically variable from cycle to cycle in ventricular arrhythmia due to atrial fibrillation (Messer et al, 1951)

The snap is of fairly high *frequency*, ranging between 75 and 250 vibrations per second, and can be recorded over a wide area of the precordium It is frequently followed by diastolic vibrations It should be distinguished from the *physiologic opening sound* (small vibration, low pitched, 0.05 to 0 07 sec distant from 2d sound), from *the 3d sound* (lower pitched, recorded only at apex, distant 0 12 to 0 18 sec from 2d sound), and from the *second (pulmonic) component of a split 2d sound* (large vibration of high frequency, recorded only or best over the 2d left interspace, separated from the *aortic component* by a shorter interval of 0 02 to 0 05 sec) The opening snap is an accentuation of *the physiologic opening sound* (Luisada, 1950) *but has* a higher pitch and is delayed It has been said (Holldack) that it takes place in cases where *the leaflets of the mitral* valve are still flexible However, it was recorded by the authors in cases with a rigid, calcified funnel. Therefore, the most likely interpretation is that of a *vibration of the valve* and not of a "creaking noise of opening" The opening snap coincides with the point O of the apex cardiogram, *the point 1 of the pneumocardiogram*, and the peak V of the jugular tracing, unless this occurs early (as in ventricular asynchronism) or

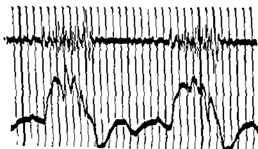


Fig 7-31. Systolic murmur over 2d right intercostal space (late diamond) and jagged tracing at suprasternal notch in a case of obstructive aortic stenosis. The large 2d sound is transmitted from the pulmonic area.

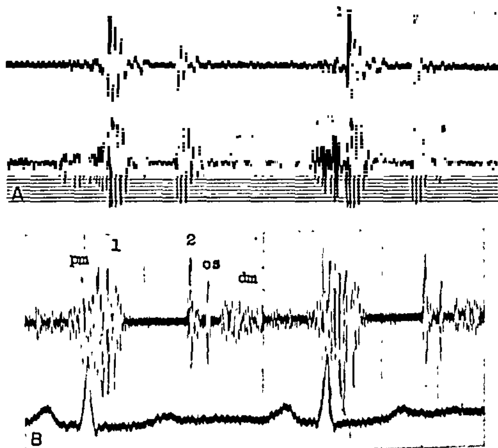


Fig. 7-25. A. Phonocardiogram at apex in a case of pure mitral stenosis with low-pitched rumbling murmur. (above) "stethoscopic" tracing; (below) filtered tracing in the band 60 to 100. Diastolic and presystolic murmur. B. Phonocardiogram at apex in a case of pure mitral stenosis with a high-pitched murmur. The tracing is a "stethoscopic" tracing. ECG for timing. Diastolic-presystolic murmur; opening snap (os); delayed 1st sound.

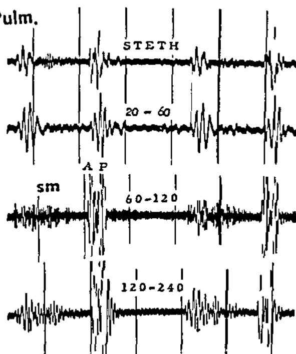


Fig. 7-26. Split 2d sound in a case of mitral stenosis. Tracing recorded over the pulmonic area with various degrees of filtration

when the diastole preceding the 1st sound was shorter (Luisada, 1940, Cossio, 1943). This is due to the fact that a short diastole is accompanied by a higher left atrial pressure. Then, it takes longer for left ventricular pressure to reach the level of the left atrium and to close the mitral valve.

3 There may be a *presystolic murmur* at, within, or above the apex. This is made of several oscillations of both low and high frequency. They occur in late diastole, increase in intensity, last until after the peak of R, and then fuse with the vibrations of the 1st sound (*murmur in crescendo*) (Fig. 7-25A, B). If the conduction time is long, the presystolic murmur may have a crescendo-decrescendo shape and be separated from the 1st sound. In extreme prolongation of P-R, this murmur may even fall in early diastole and be indistinguishable from an average diastolic murmur. This murmur disappears if there is atrial fibrillation. Selective phonocardiography with variable bandpass filters reveals that the most

other cases, there is a brief interval between *2d sound* and beginning of the murmur, and *the murmur* has a *crescendo-decrescendo pattern coinciding* with the phase of rapid filling (Wells et al., 1949) (Fig. 7-28) The murmur sometimes ends in early diastole; in most cases, it continues with small vibrations throughout all diastole. If the murmur is musical, the vibrations are regular and present a "concertina-like" appearance.

The use of filters makes it possible to record the murmur with a magnitude comparable *to that of auscultation* (Luisada et al, 1955). The most important vibrations are between 150 and 250 cps. Higher-pitched vibrations can be recorded in most cases between 250 and 500, and occasionally even between 500 and 1,000 cps However, the higher the pitch, the smaller the magnitude, so that those vibrations can be demonstrated only with tremendous amplification and contribute little to the over-all graphic (and auscultatory) picture (Butterworth et al; Luisada et al, 1955).

The 1st sound may be small or prolonged because of myocardial lesions. There may be a high vibration (*aortic opening click*) which *either coincides with the rise of the carotid* pulse or slightly follows it. If it coincides

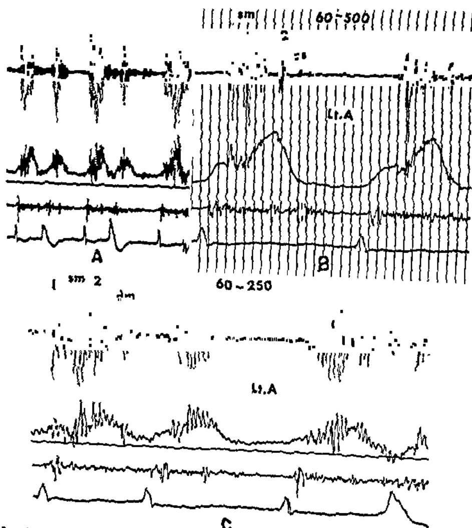


Fig. 7-33. Intracardiac pressure curves and intracardiac phonocardiograms from left atrium in a case of pure mitral insufficiency. From above· intracardiac phonocardiogram, pressure curve, extracardiac phonocardiogram, ECG A 50 mm/sec speed. B. 100 mm/sec speed, needle. C. 100 mm/sec speed, catheter near the mitral valve Large systolic murmur. Opening snap. (From Luisada et al Am. J. Card. 1958)

significant vibrations are usually between 60 and 100, with additional overtones between 100 and 200 and undertones between 30 and 60 vibrations per second. This murmur is caused by the presystolic acceleration of flow due to left atrial contraction and vibrations which set up in the blood of the left ventricle.

4. There may be a rumbling *diastolic murmur* at or near the apex (Fig. 7-25). This is revealed by a series of irregular, small, usually low-pitched vibrations. They start soon after the opening snap (see below) and continue until mid-diastole or late diastole, first increasing and then decreasing in amplitude. If diastole is long, there may be a pause between this murmur and the presystolic murmur; otherwise the two merge A larger vibration may be recognized within the first part of the murmur. This is a 3d sound of the left ventricle (or, possibly, of the right ventricle). The frequency range of the diastolic murmur is about the same as that of the presystolic murmur, but with fewer overtones (lower-pitched murmur). This murmur is caused by the acceleration of flow which takes place during the phase of passive rapid filling and which causes vibrations in the blood of the left ventricle. The use of a variable bandpass filter makes it possible to amplify the most significant vibrations and accurately to study cases with questionable diastolic vibrations

5. The *opening snap of the mitral valve* is a typical vibration which, alone, is sufficient to diagnose a mitral lesion, usually (but not always) a mitral stenosis (Fig. 7-25B). It is a rapid vibration which is separated from the main vibration of the 2d sound by an interval of 0.07 to 0.12 sec. As known, *the interval 2-OS measures the isometric relaxation period* and is prolonged in mitral stenosis (normally, it measures 0.05 to 0.08 sec) (Wells) The prolongation is due to the fact that the rigid mitral valve resists opening; however, as the high level of left atrial pressure tends to

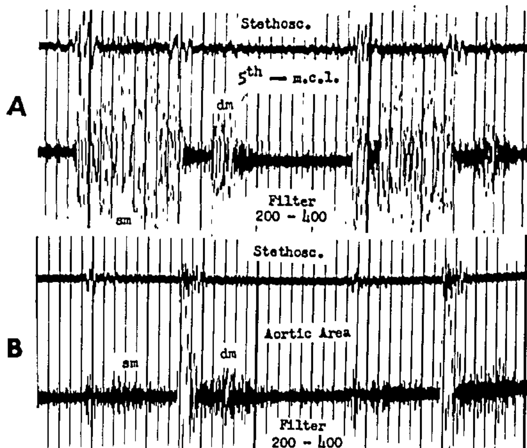


Fig. 7-29. Phonocardiograms in a case of rheumatic heart disease with aortic insufficiency, minimal aortic stenosis, and minimal mitral stenosis (left heart catheterization). The "filtered" tracing at the apex (A) shows a systolic murmur in crescendo, evidence of mitral insufficiency. The "filtered" tracing of the aortic area (B) shows a moderate systolic and a large diastolic murmur, evidence of aortic insufficiency.

PHONOARTERIOGRAMS. These tracings can be recorded over various arteries and may reveal the following data (Luisada, 1943):

1 There may be a single, large vibration during the expansion of the artery (*pistol-shot sound*).

2. There may be two sounds, one during the expansion, one during the collapse of the artery, prior to the dicrotic wave (*double sound of Traube*).

3 There may be two murmurs which replace the two above sounds and are favored by compression of the vessel (*double murmur of Duroziez*). It seems likely that they are caused by a double forward motion of the blood.

Aortic Stenosis. The phonocardiogram gives evidence of the typical systolic murmur, which is revealed by a series of irregular vibrations of medium and high frequencies (*coarse murmur*). The vibrations typically increase during ejection, then decrease, giving the pattern of a *diamond-shaped murmur* (Figs 7-30 to 7-32) This murmur is present in organic aortic stenosis (*obstructing aortic stenosis*), in cases with minimal deformity of the leaflets (*nonobstructing aortic stenosis*), and in cases with dilatation of the ascending aorta caused by atherosclerosis or aortitis (*relative aortic stenosis*) Typical, obstructing aortic stenosis often causes a murmur with a late peak (*late diamond*) or even a crescendo-type in late systole, while nonobstructing or relative aortic stenosis usually causes a murmur having a peak before the middle of systole (*early diamond*) (Aravanis and Luisada, 1957) (Fig 7-30A) This is not true in most children, probably because many of them have a *subaortic stenosis*, and this, even though obstructive, causes an early diamond type murmur (lower obstruction) (Nadas)

In the obstructive type, the 2d aortic sound is typically *small* and may be delayed, so that it may occur *after* the pulmonic 2d sound (*paradoxical splitting*—Leatham) (Fig 7-32) In certain cases, the best recording of the aortic component of the 2d sound is obtained over the 1st right interspace, where the pulmonic component is poorly transmitted

A tracing of *the suprasternal notch* records the systolic murmur as well as, or better than, a tracing of the 2d right interspace In certain cases, on the other hand, the best tracing is obtained over the 3d left interspace

PHONOARTERIOGRAMS Carotid tracings reveal large vibrations during the passage of the pulse These are partly transmitted from the aortic area and partly due to turbulence of the blood Even though this arterial murmur is larger in obstructive stenosis, it can be recorded also in the other forms

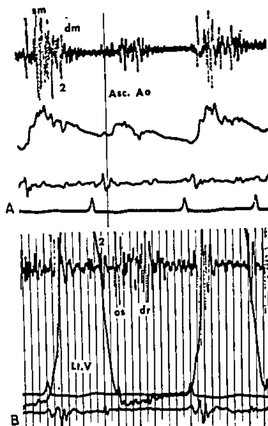


Fig. 7-35. A Intraaortic phonocardiogram in a case of aortic stenosis and insufficiency and mitral stenosis Large diamond-shaped systolic murmur, short diastolic murmur. B Intracardiac phonocardiogram (left ventricle). Large diastolic rumble and opening snap (From Luisada et al Am. J Card. 1958)

Tricuspid Insufficiency. Tracings recorded over the 3d left interspace and over the 3d right interspace reveal the vibrations of a *systolic murmur* The latter is either *in decrescendo* or *continuous* It is frequently high-pitched and becomes larger in the inspiratory apnea (*Chavez and Rivero Carvallo*) Thus, comparison between tracings recorded in inspiratory and expiratory apnea permits differentiation from a mitral murmur, which is larger in the expiratory apnea, increased blood inflow into the right ventricle in inspiration explains the behavior of this murmur.

Tricuspid Stenosis. The phonocardiogram may reveal a diastolic murmur over the tri-

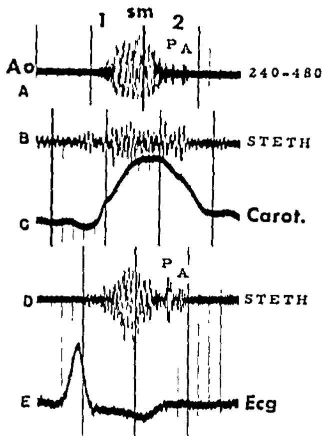


Fig. 7-32. Superimposed tracings in a case of calcific aortic stenosis. A, B. Phonocardiograms are recorded over the aortic area. C Tracing is recorded over the carotid artery. D. Diamond-shaped systolic murmur Paradoxical splitting of the 2d sound. The aortic component coincides with the incisura of the carotid tracing.

late (either for the same reason or because of technical errors).

6. It is common to observe the vibrations of a *systolic murmur at the pulmonic area* (Fig. 7-26). Curiously enough, these vibrations are frequently larger in the early stages of the disease, unless severe dilatation of the pulmonary artery, due to pulmonary hypertension, occurs later.

7. There frequently is a *split 2d sound* (Fig. 7-26). The distance between the two components of this split sound varies from 0 04 to 0.06 sec. Very seldom is the splitting audible when the interval is below 0 03 sec The large pulmonic component always follows the aortic component.

8. There may be an *early-diastolic murmur in decrescendo* at the pulmonic area due to pulmonic insufficiency (*Graham Steell murmur*). This murmur usually appears during congestive failure and disappears with recovery. A similar, but persistent, murmur indicates sclerotic or endocarditic pulmonic insufficiency (Luisada and Wolff). An aortic diastolic murmur in this region is, of course, extremely common.

9. When no murmur is audible in a case of mitral stenosis (*silent or mute mitral stenosis*), either no murmur is recorded (rare) or there are low-pitched, inaudible vibrations during diastole (*subliminal murmur*). In both cases, the murmur may appear or become audible after exercise or with the patient in the left decubitus. The lack of murmur can be explained by the length of diastole, which enables the blood to pass slowly from the left atrium to the left ventricle with a minimum of vibrations. This "mute" mitral stenosis is occasionally found in patients with atrial fibrillation (no presystolic murmur), strongly digitalized (long diastoles), and having no opening snap.

Relative Mitral Stenosis. Whenever the left ventricle is severely dilated, the blood penetrating through the mitral valve creates eddies which cause a rumbling diastolic murmur. This can be recorded in cases of rheumatic carditis, coronary or hypertensive heart disease (Fig 7-27), or anemia. Differentiation should be based on the following data:

1. No opening snap, no prolongation of the Q–1st sound interval.

2. The murmur starts late in diastole, usually after a large 3d sound.

3. The vibrations are larger than in organic mitral stenosis and may be larger than the heart sounds

a

those of organic mitral stenosis.

Aortic Insufficiency. Tracings recorded over the area of greatest intensity of the murmur (either 2d right interspace or 3d left interspace) show that the main vibration of the 2d sound is followed by a series of other vibrations of high frequency The latter are usually of small magnitude in comparison with the auditory impression and decrease gradually in diastole. When a ruptured, perforated, or everted aortic valve is the cause of regurgitation, the vibrations are larger and regular (*musical murmur*). The characteristics of the diastolic murmur vary. In some cases, the vibrations start with the 2d sound and gradually decrease (*murmur in decrescendo*). In

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The low-frequency tracings of the precordium and the arterial and venous pulses in rheumatic heart disease

ALDO A. LUISADA AND EUGENIO JONA

LOW-FREQUENCY TRACINGS

Mitral Insufficiency. The low-frequency tracing *of the apex* often shows the following changes.

1. A high wave in early systole, there is a quick rise followed by a sudden drop before the end of the 1st sound.

2. A low level of the point 0, at times, high waves are seen during diastole (both waves 3 and 4 are high)

Low-frequency tracings recorded *outside the apex* (regional cardiograms) may show the following data:

1. A high atrial wave (*wave 4*) over the midprecordium (strong left atrial contraction)

2. A high vascular wave (*wave p*) at the 2d left interspace (high pulmonic pulsation)

The *epigastric tracing* may present a *chiefly negative wave* during ejection. This, together with the high positive wave at the apex, indicates predominant enlargement of the left ventricle.[1]

Mitral Stenosis. The low-frequency tracing of the *apex* (apex cardiogram) may reveal the following phenomena (Fig 7-37A):

[1] Compare these data with those of normal individuals (Part 3, Chap 7)

1. In systole, a *slow rise* of the tracing during the tension period with a *delay of the peak 1a* (delayed closure of the mitral valve). There may be a negative wave

2. *In diastole*, a slow descent of the tracing after the 2d sound (delayed opening of the mitral valve) and *a slow rise* afterward (slow filling in early diastole), also, a small atrial wave in the apical tracing (difficult filling of the left ventricle), or no atrial wave.

The low-frequency tracing of the *2d left interspace* (*regional cardiogram*) *often reveals* a high systolic wave (large pulsation of the pulmonary artery), that recorded over the 3d left interspace *may present* a high atrial wave (large pulsation of the left atrium).

The *epigastric tracing* frequently shows a high atrial wave (large pulsation of the right atrium) and a *high positive pulsation in systole* The latter, together with a short positive wave followed by a negative one, or with a negative pulsation at the apex, indicates right ventricular enlargement (Part 3, Chap 7).

Aortic Insufficiency. The low-frequency tracing of the *apex* shows a high early systolic wave followed by a deep depression during most of ejection. This is the "choc en dôme"

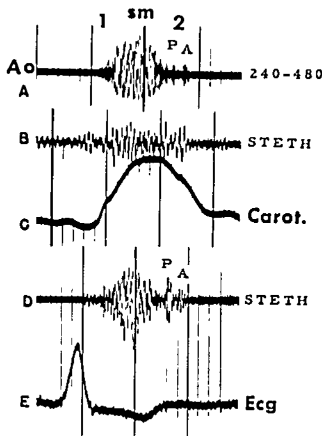


Fig. 7-32. Superimposed tracings in a case of calcific aortic stenosis. A, B. Phonocardiograms are recorded over the aortic area. C. Tracing is recorded over the carotid artery. D. Diamond-shaped systolic murmur. Paradoxical splitting of the 2d sound. The aortic component coincides with the incisura of the carotid tracing.

late (either for the same reason or because of technical errors).

6 It is common to observe the vibrations of a *systolic murmur at the pulmonic area* (Fig 7-26). Curiously enough, these vibrations are frequently larger in the early stages of the disease, unless severe dilatation of the pulmonary artery, due to pulmonary hypertension, occurs later.

7. There frequently is a *split 2d sound* (Fig 7-26). The distance between the two components of this split sound varies from 0 04 to 0.06 sec. Very seldom is the splitting audible when the interval is below 0 03 sec The large pulmonic component always follows the aortic component

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Relative Mitral Stenosis. Whenever the left ventricle is severely dilated, the blood penetrating through the mitral valve creates eddies which cause a rumbling diastolic murmur. This can be recorded in cases of rheumatic carditis, coronary or hypertensive heart disease (Fig 7-27), or anemia. Differentiation should be based on the following data:

1. No opening snap, no prolongation of the Q–1st sound interval

2. The murmur starts late in diastole, usually after a large 3d sound.

3. The vibrations are larger than in organic mitral stenosis and may be larger than the heart sounds

4. The vibrations can often be recorded over a large area of the precordium in contrast with those of organic mitral stenosis.

Aortic Insufficiency. Tracings recorded over the area of greatest intensity of the murmur (either 2d right interspace or 3d left interspace) show that the main vibration of the 2d sound is followed by a series of other vibrations of high frequency The latter are usually of small magnitude in comparison with the auditory impression and decrease gradually in diastole When a ruptured, perforated, or everted aortic valve is the cause of regurgitation, the vibrations are larger and regular (*musical murmur*). The characteristics of the diastolic murmur vary In some cases, the vibrations start with the 2d sound and gradually decrease (*murmur in decrescendo*). In

(*anacrotic notch*), the pulse is called *anacrotic pulse* (Fig. 7-38B) If recorded at the suprasternal notch or on the carotid arteries, the pulse tracing may show a series of vibrations which reveal the turbulence of flow and are the equivalent of a *thrill* (so-called *carotid shudder*). The aortogram at the suprasternal notch

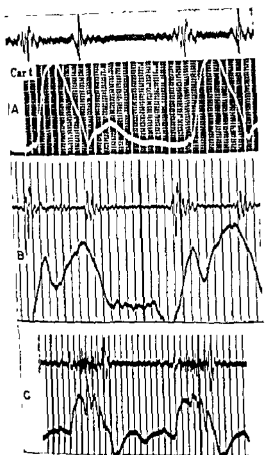


Fig. 7-38. A. Pulsus celer of aortic insufficiency. B. Pulsus tardus with a marked anacrotic notch in aortic stenosis C Aortogram at suprasternal notch revealing pulse with several peaks

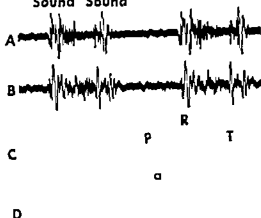


Fig. 7-40. Giant A wave in the jugular tracing (D) of a case of tricuspid stenosis Superimposed are phonocardiograms at pulmonic (A) and aortic (B) areas and ECG (C)

often reveals a pulse with two or three peaks (Fig. 7-38C)

Tricuspid Insufficiency. The *venous tracings* (jugular, hepatic) are the most revealing in this defect They have been studied by McKenzie (1902) and, more recently, by a score of authors including White and Cooke, Groedel, and Messer et al Both venous tracings show a high positive wave in presystole unless there is atrial fibrillation. During systole, the systolic collapse is substituted by a *systolic plateau* which resembles a tracing of intraventricular pressure This pattern is typical in both organic and "relative" insufficiency (Fig 7-39) As organic insufficiency is frequently associated with some degree of stenosis and some change in pattern, an *early plateau* is more commonly encountered in "functional" tricuspid insufficiency while a *late plateau* is

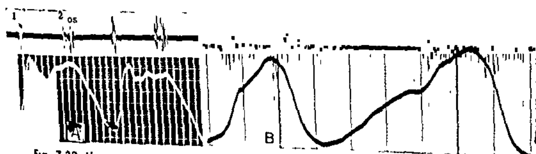


Fig. 7-39. Venous tracings in two cases of tricuspid insufficiency revealing a "systolic plateau" A. Hepatic tracing B Jugular tracing

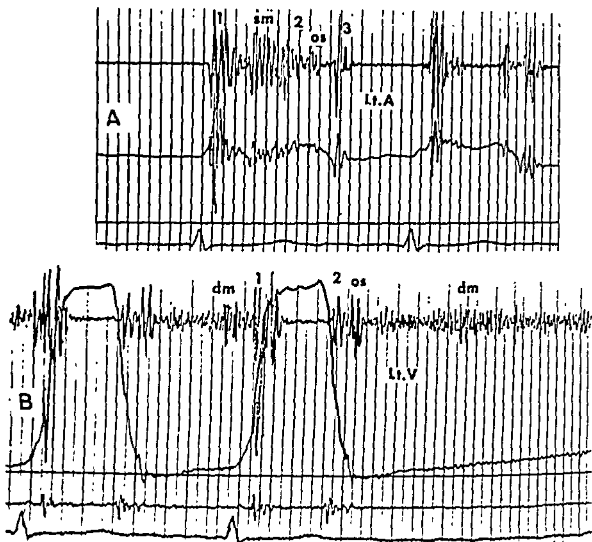


Fig. 7-34. Intracardiac phonocardiograms in a case of mitral insufficiency and stenosis. A Left atrial tracings Large systolic murmur Opening snap B. Left ventricular tracings. Opening snap, diastolic murmur. Tracings as in Fig. 7-33. (From Luisada et al. Am. J. Card. 1958)

with the foot of the pulse (Wolferth and Margolies), it is an *opening click* of the aortic valve.[2] If it follows it (Cossio et al., 1943), it is due to the systolic distention of the dilated aorta.

Vibrations due to a *systolic murmur* are common (Figs 7-28 and 7-29). They are similar to those caused by organic or relative aortic stenosis and may often be correctly interpreted on the basis of the configuration of the murmur (see Aortic Stenosis).

Studies by the author on the *Austin Flint murmur* have revealed the following facts

1. In some cases, there is a *triple rhythm* The loud 4th (atrial) sound in presystole is erroneously mistaken for a presystolic murmur.

2. In other cases, there is a low amplitude of the first part of the 1st sound followed by a snapping vibration (aortic opening click). If there is intraventricular block or BBB, the 1st sound is even more abnormal. The low vibrations which initiate the 1st sound are erroneously taken for a presystolic murmur, while the click is considered the mitral closing snap

3. In other cases, low-pitched systolic vibrations, arising in the aorta, are louder than the 1st sound and may be mistaken for it The 1st sound then is mistaken for a presystolic murmur

Therefore, in all the above cases, either there is a triple rhythm or the presystolic murmur is due to an auscultatory illusion (Luisada, 1944). Subsequent studies (Luisada et al., 1950, 1955) have shown that, in certain cases, the phonocardiogram actually reveals a *diastolic rumble* which may be mistaken for that of mitral stenosis However, several graphic data can be used in most cases to differentiate this "functional" murmur from that of carditis or hypertensive or coronary heart disease (see Relative Mitral Stenosis).

[2] This was called "ejection sound" by Leatham.

(*anacrotic notch*), the pulse is called *anacrotic pulse* (Fig. 7-38B) If recorded at the suprasternal notch or on the carotid arteries, the pulse tracing may show a series of vibrations which reveal the turbulence of flow and are the equivalent *of a thrill (so-called carotid shudder*). The aortogram at the suprasternal notch often reveals a pulse with two or three peaks (Fig 7-38C)

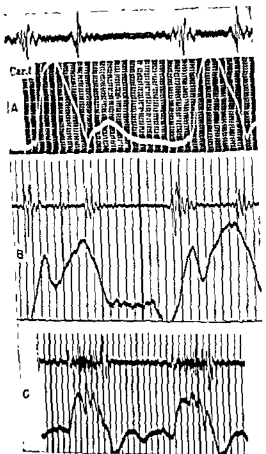


Fig. 7-38. A. Pulsus celer of aortic insufficiency. B. Pulsus tardus with a marked anacrotic notch in aortic stenosis C *Aortogram at suprasternal notch revealing pulse with several peaks.*

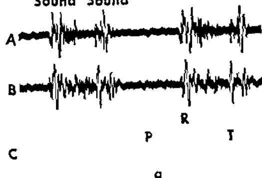


Fig. 7-40 Giant A wave in the jugular tracing (D) of a case of tricuspid stenosis Superimposed are phonocardiograms at pulmonic (A) and aortic (B) areas and ECG (C).

Tricuspid Insufficiency. The *venous tracings* (jugular, hepatic) are the most revealing in this defect They have been studied by McKenzie *(1902) and, more recently, by a score* of authors including White and Cooke, Groedel, and Messer et al Both venous tracings show a high positive wave in presystole unless there is atrial fibrillation During systole, the systolic collapse is substituted by a *systolic plateau* which resembles a tracing of intraventricular pressure This pattern is typical in both organic and "relative" insufficiency (Fig 7-39) As organic insufficiency is frequently associated with some degree of stenosis and some change in pattern, an *early plateau* is *more commonly encountered in "functional"* tricuspid insufficiency while a *late plateau* is

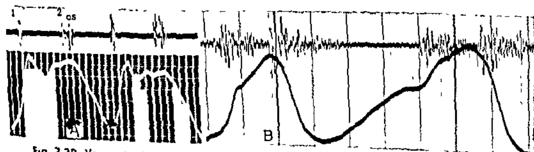


Fig 7-39. Venous tracings in two cases of tricuspid insufficiency *revealing a "systolic plateau."* A. Hepatic tracing B Jugular tracing.

cuspid area which is similar to the mitral apical murmur in mitral stenosis. Thus, a *tricuspid opening snap* and a *diastolic-presystolic rumble* may be recorded. Again, inspiration or inspiratory apnea reveals an accentuation of the murmur, in contrast with the behavior of a mitral murmur (Rivero Carvallo). This differential diagnosis is particularly necessary because, in nearly all cases, tricuspid stenosis occurs in association with mitral stenosis.

Relative tricuspid stenosis occurs in cases with severe enlargement of the right ventricle and a normal tricuspid valve. The phonocardiogram reveals the vibrations of a diastolic rumble which is of large amplitude, starts with a 3d sound, and becomes larger in inspiration.

INTRACARDIAC PHONOCARDIOGRAMS

Intracardiac phonocardiographic tracings of the left heart have been recorded by Luisada et al. (1958) in 17 cases of rheumatic heart disease. Interesting data were collected. The systolic murmur of *mitral insufficiency* is maximal within the left atrium, especially in the vicinity of the mitral valve (Figs. 7-33 and 7-34A). The opening snap and the diastolic murmur of *mitral stenosis* are recorded best within the left ventricle (Figs. 7-34B and 7-35B). The diastolic murmur of *aortic insufficiency* is best recorded in the left ventricle, while that of *aortic stenosis* is maximal in the aortic arch (Fig. 7-35A).

Further studies of *tricuspid insufficiency* revealed the typical systolic murmur transmitted to the right atrium and the large veins. A large early diastolic murmur was recorded only in the venae cavae and was attributed to the tumultuous flow of blood which is typical of that phase, after the end of the phase of regurgitation (Fig 7-36).

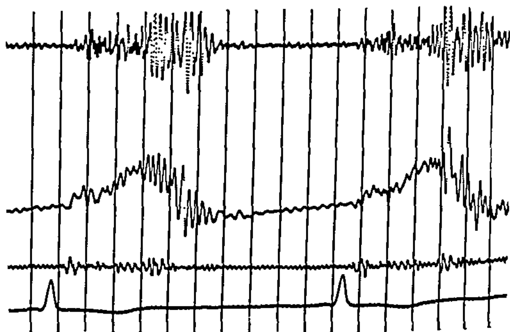


Fig. 7-36. Phonocardiogram within the inferior vena cava in a case of severe organic tricuspid insufficiency Tracings as in Fig. 7-33.

(*anacrotic notch*), the pulse is called *anacrotic pulse* (Fig 7-38B). If recorded at the suprasternal notch or on the carotid arteries, the pulse tracing may show a series of vibrations which reveal the turbulence of flow and are the equivalent of a *thrill* (so-called *carotid shudder*). The aortogram at the suprasternal notch often reveals a pulse with two or three peaks (Fig. 7-38C)



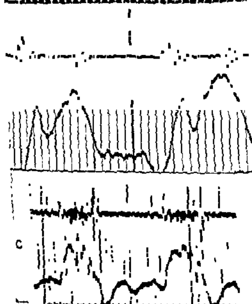


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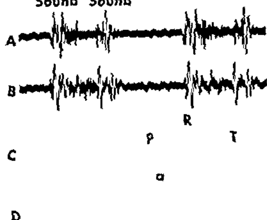


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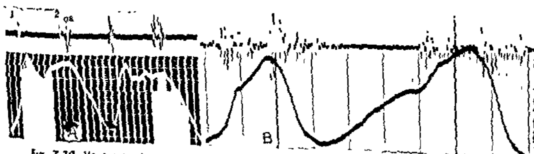


Fig 7-39 Venous tracings in two cases of tricuspid insufficiency revealing a "systolic plateau" A. Hepatic tracing. B. Jugular tracing.

of earlier authors (Fig. 7-37B). In certain cases, however, a high systolic plateau is present. If the record is taken *outside* the apex, a deep systolic depression is often recorded. The atrial wave is often high in syphilitic and atherosclerotic forms. Rapid filling is often revealed by a high wave in early diastole; if marked, this is typical and is due to blood regurgitating from the aorta and increasing the rapidity of filling.

AORTOGRAMS. These tracings (Part 3, Chap. 4) reveal a high systolic wave (large aortic pulse).

The low-frequency tracing of the *epigastrium* usually reveals a *negative* systolic plateau which, together with the large pulsation of the apex, indicates left ventricular enlargement (Part 3, Chap 7).

Aortic Stenosis. The low-frequency tracing of the apex reveals that the ascending part of the systolic impulse is either slow or double ("camel-back" or "staggered" pattern). The systolic thrill is accompanied by a series of vibrations which are typical in tracings recorded at the suprasternal notch (Fig. 7-38C)

Tricuspid Insufficiency. The tracing of the apex has a retraction or *backward thrust* during ventricular systole, followed by a forward thrust in diastole (Fig. 7-37C). On the contrary, there is a *forward thrust at the epigastrium, the lower part of the sternum,* and *the right precordium* (Dressler). This double movement creates a *seesaw motion* and is due to the regurgitant jet into the large veins and the liver, and to the suction effect it creates in the chest, as well as the effect of right ventricular enlargement.

ARTERIAL AND VENOUS TRACINGS

Aortic Insufficiency. The typical tracing of the arterial pulse presents a rapid rise, a rapid drop, and a small dicrotic wave (Fig. 7-38A) The rapid drop of the carotid tracing occurs still in systole, as pointed out by Starling and, therefore, is only indirectly connected with the valvular defect. Actually, it is due to the great rapidity with which the pulse moves in an arterial system depleted by the regurgitation. A comparison of tracings recorded over various arteries reveals a rapid transmission of the pulse wave.

Aortic Stenosis. The pulse tracing shows an ascending phase which is slower than normal. As this phase is often marked by a depression

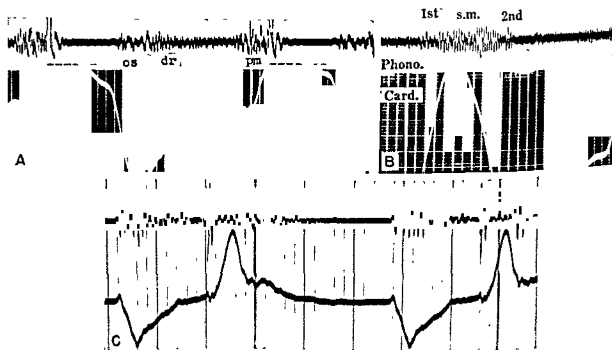


Fig 7-37. A Phonocardiogram (above) and low-frequency tracing of the apex (below) in a case of mitral stenosis The low-frequency tracing reveals a typical slow rise in the phase of "rapid" filling (early diastole) B. Phonocardiogram (above) and low-frequency tracing of the apex (below) in a case of aortic insufficiency (*choc en dôme*) C Phonocardiogram (above) and low-frequency tracing of the apex (below) in a case of tricuspid insufficiency Backward thrust in systole and forward thrust in diastole.

The electrokymogram in rheumatic fever and rheumatic heart disease

ALDO A. LUISADA AND OLGA M. HARING

RHEUMATIC FEVER

Electrokymograms of the left atrium in acute rheumatic fever have been studied by Luisada and Magri. Some cases of rheumatic fever with a systolic murmur present a normal tracing, others present evidence of moderate mitral regurgitation (early rise in systole). The great majority present a *plateau-like pattern* (Fig. 7-41), indicating systolic distention of the atrium due to transmission of intraventricular pressure on account of mitral insufficiency This may very well be due to myocardial damage (so-called *functional regurgitation*) and does not imply a lesion of the valvular leaflets Repeated EKy examinations were found useful by the authors in the evaluation of myocardial and valvular lesions.

RHEUMATIC HEART DISEASE

Mitral Insufficiency. The EKy of the left atrium is of importance for diagnosis It should be recorded as a *border tracing* (left auricular appendage, left atrium in the two obliques at two levels each, left lateral at two levels) and as a *densogram* (Part 4, Chap 11). The normal tracing of the left atrium consists of a sharp negative wave in presystole (inward motion–atrial contraction) and a more rounded negative wave in systole (inward motion–lowering of AV septum) In cases of mitral insufficiency, a new pattern is visible (Luisada and Fleischner, 1948, Haring et al, 1955, Luisada and Liu, 1958). The following data can be observed:

1. The presystolic negative wave is deeper and broader (unless there is atrial fibrillation) on account of stronger atrial contraction

2. The normal systolic negative wave disappears and is substituted by one of the following patterns:

a An *oblique line* rapidly rising and



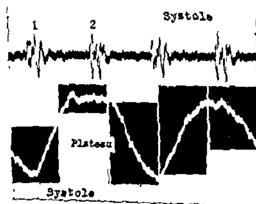


Fig. 7-41. Electrokymograms of the left atrium (border tracings) in two cases of acute rheumatic fever (first attack). (From Luisada and Magri. Am. J. Med. 1953.)

of earlier authors (Fig. 7-37B). In certain cases, however, a high systolic plateau is present. If the record is taken *outside* the apex, a deep systolic depression is often recorded. The atrial wave is often high in syphilitic and atherosclerotic forms. Rapid filling is often revealed by a high wave in early diastole; if marked, this is typical and is due to blood regurgitating from the aorta and increasing the rapidity of filling.

AORTOGRAMS. These tracings (Part 3, Chap. 4) reveal a high systolic wave (large aortic pulse).

The low-frequency tracing of the *epigastrium* usually reveals a *negative* systolic plateau which, together with the large pulsation of the apex, indicates left ventricular enlargement (Part 3, Chap. 7).

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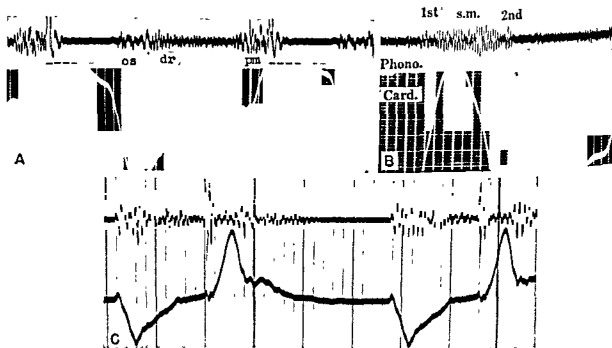


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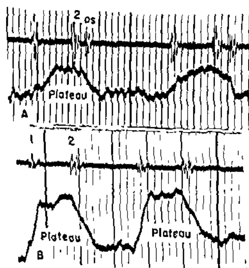
therefore, the EKy often causes overestimation of the degree of regurgitation in comparison with a pressure tracing of the left atrium (Luisada and Liu). A recent attempt has been made in the author's laboratory to calibrate the EKy by means of a roentgenkymogram.

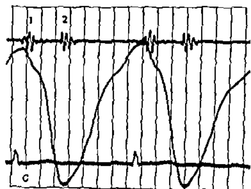
Aortic Insufficiency. The border tracing of the aortic arch reveals a rapidly expanding and rapidly collapsing pulse with a decrease of all the secondary landmarks, including the dicrotic wave (Fig 7-43D).

The border tracings of the left ventricle show a pulsation made by a rapid drop (rapid ventricular contraction) and a rise in early diastole which is faster than in normal subjects (Fig. 7-43C). The latter is due to the fact that the left ventricle is distended by two streams, the normal coming from the left atrium and the abnormal due to aortic regurgitant blood.

Aortic Stenosis. The border tracing of the aortic knob presents an *anacrotic depression* similar to that exhibited by the carotid pulse. The border tracing of the left ventricle reveals abnormalities of contraction similar to those exhibited by the apex cardiogram.

Tricuspid Insufficiency. The border tracing of the right atrium may show a plateau pattern similar to that revealed by the left atrium in mitral insufficiency. However, in the experience of the authors (and also in that of Dussaillant), this pattern is seldom so revealing as that presented by jugular or hepatic pulse tracings.





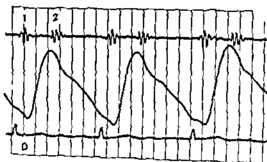


Fig. 7-43. Electrokymograms of left atrium in a case of mitral valve disease with insufficiency and stenosis A *"plateau pattern"* is present It is a "late plateau" before surgery (A) but becomes an "early plateau" after surgery (B) on account of more severe insufficiency. (*From Haring et al Am. Heart J* 1956.) C Left ventricular EKy in a case of aortic insufficiency D Aortic EKy *in the same case.*

more typical of organic insufficiency (Messer et al.).

In graphic tracings, it is easy to differentiate an "expansive" pulsation of the liver from a transmitted pulsation of the right heart. The latter is maximal at the epigastrium, is extremely rapid, and is limited to the first third of ventricular systole. An intrinsic pulsation of the liver, evidence of tricuspid regurgitation, is maximal at the right flank, is less rapid in its onset, and lasts throughout all of ventricular systole and slightly beyond the end of this phase, i.e., until the opening of the tricuspid valve in early diastole.

Tricuspid Stenosis. The *venous tracings* reveal only a *high A wave* if there is a "pure" stenosis and the patient still has a sinus rhythm (Fig. 7-40). If there is no venous engorgement, this wave may be recorded only on the jugular bulb and not more distally (Puddu). This large wave has no diagnostic value because it may be present in patients having heart failure and right atrial hypertension or in cor pulmonale.

If tricuspid stenosis is associated to some degree of insufficiency, a typical plateau pattern is observed. In contrast with the early plateau of pure insufficiency (whether organic or relative) this has a *late-plateau type;* it starts with a slow rise, has a flat top, and is followed by a slow drop in early diastole.

resistances, but usually persistent, repeated wedging in different locations will ultimately give a satisfactory pressure with an atrial wave form (Fig. 7-44), and arterialized blood may be drawn from the catheter.

Cardiac output is determined either immediately before or after determination of the wedge pressure This pressure, after an assumed left ventricular diastolic pressure of 5 mm Hg is subtracted from it, is entered into the hydraulic formula (Gorlin and Gorlin, Part 4, Chap. 12) along with the simultaneously recorded cardiac output and diastolic filling period measured from the systemic arterial pressure pulse. Mitral valve area is calculated The patient is then instructed to perform leg exercise The pulmonary wedge pressure is recorded continuously or intermittently until it has stabilized—this usually takes about 2 min A precipitous rise in this pressure with maintenance of atrial wave form is in itself usually an indication of severe mitral stenosis During exercise, cardiac output, heart rate, and diastolic filling period are again measured as close as possible in time to the wedge pressure or during another similar period of exercise Once again, valve area is calculated.

The author has found this particular type of study extremely rewarding It has been possible to obtain duplicate values for valve areas When simultaneous left heart catheterization has been done, the calculations for valve area have not varied strikingly between the two techniques of measuring pressure gradients

DETERMINATION OF DEGREE OF PULMONARY VASCULAR RESISTANCE It is well known that, in mitral stenosis, the pulmonary vascular resistance frequently is increased This increase is related to intimal and medial thickening, narrowing due to arterial spasm, thrombosis and actual necrosis within the vessel walls This change is expressed physiologically as an increase in the resistance to blood flow across the precapillary area With an increase in resistance, either blood flow must fall or the pressure gradient across the narrow vascular bed must be increased

In mitral stenosis, presumably, the pulmonary vascular lesion arises in relation to the chronically elevated pulmonary capillary pressure The degree of obstruction in terms of the pressure load imposed on the right heart may actually exceed that which is due to the mitral valve obstruction As a result, this vascular obstruction may have more effect on the heart and lungs and, therefore, on the prognosis of surgical therapy than almost any other factor In many individuals, the presence of an increased pulmonary vascular resistance may be suspected from the ECG and the x-ray contour of the heart and large pulmonary vessels. In some individuals, however, it is not possible to tell adequately whether the obstruction is primarily valvular or primarily pulmonary. The vascular lesion affects pulmonary parenchyma, with resultant alterations in ventilation-perfusion ratio and alveolo-capillary diffusion. The presence of a pulmonary factor frequently considerably affects the operative and postoperative management

In many patients, therefore, it becomes imperative to assess the degree of *pulmonary hypertension* resulting from secondary pulmonary arteriolar disease. To do so, it is necessary to know the pressure proximal and distal to the vascular obstruction. After the pulmonary arterial pressure is recorded, an attempt is made to record pulmonary wedge pressure, or else left atrial pressure is measured during simultaneous left heart catheterization. Measurement of the pressure only proximal to an obstruction gives no indication of where the resistance is located This is certainly true in mitral stenosis However, because of the nature of pulmonary capillaries and the relation of intravascular pressure to colloid osmotic pressure of plasma, *it would be most unusual for the pulmonary capillary pressure to be much higher than 30 mm Hg*

In actual practice then, when it is physically impossible to obtain a postarteriolar pressure, and the diagnosis of mitral stenosis has been determined by other criteria, one may consider the pulmonary vascular gradient as pulmonary arterial mean pressure minus 30 mm Hg. It should be emphasized, however, that this can be done only in the presence of severe pulmonary hypertension, where the vascular gradient would be 15 to 40 mm Hg or more. In general, a good effort should be made to obtain postarteriolar pressure.

To measure resistance, it is also necessary to know the *rate of blood flow* through the area under investigation The most convenient technique is to measure the cardiac output by *either the direct Fick* or an indicator-dilution

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reaching its peak slightly before or at the 2d sound (*I* wave, slightly preceding, or fused with, the *V* wave). (Fig. 7-42A.)

b. A *systolic plateau* with a rapid rise in early systole, an oblique rise during the rest of systole, and *a rapid drop* soon after the 2d sound (*early plateau*, Fig. 7-42B).

Pattern *a* is similar to a tracing of left atrial pressure in the same cases (Fig. 7-42A). Pattern *b* is more common in patients with severe tachycardia or atrial fibrillation. In some cases with fibrillation, the plateau may be visible only when a contraction is preceded by a short diastole. It is the graphic expression of a "systolic swelling" of the left atrium caused by the regurgitant jet. It is similar to a tracing of intraventricular pressure and to a tracing of left atrial pressure in animals with experimental mitral insufficiency (Haring et al.) or in patients with early rheumatic carditis (Luisada and Magri). It is usually similar to a *tracing of left atrial pressure* (Luisada and Liu; Judge et al.) (Fig. 7-42B). However, it may happen that systolic distention of a left atrium with a normal diastolic pressure (pure regurgitation) causes a plateau pattern in the EKy while the pressure tracing rises more slowly. This seems due to elastic distention of the wall, which prevents the pressure from rising too rapidly. It may also happen that several positions reveal the typical pattern while one or two do not. It is likely, though not proved, that this indicates moderate regurgitation.

The EKy of the *pulmonary veins* presents two typical changes:

1. A high and broad positive wave in presystole, equivalent to the A wave of the jugular tracing.

2. A high positive plateau in systole, the result of increased pressure and transmissions of the plateau-like pattern from the left atrial cavity. It reveals the fact that, during systole, the blood cannot flow from the pulmonary veins into the left atrium and causes venous engorgement similar to that of the venae cavae in tricuspid insufficiency.

Mitral Stenosis. In mitral stenosis, the EKy of the left atrium may have a perfectly normal pattern. This is explained by the fact that the *pressure pattern* of this chamber may be completely unaltered while all waves are shifted to a higher *pressure level* by the mitral obstruction. However, it is very common that moderate or severe mitral stenosis is associated with minimal or moderate insufficiency. In these cases, the EKy reveals a high *systolic plateau* which is somewhat different from that of pure mitral insufficiency: its rise is more oblique; it reaches its top at about one-third systole; *its drop starts with the opening snap and is slow and oblique*. This is the *late-plateau pattern* (Haring et al.; Judge et al.) (Figs. 7-42B and 7-43A). It is unfortunate that lack of an exact and practical system of calibration prevents evaluating the height of this plateau,

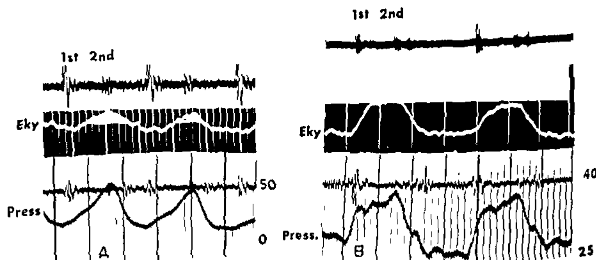


Fig. 7-42. Comparison of EKy of the left atrium with the pressure curve of the same chamber in cases of rheumatic mitral lesions A Pure insufficiency B Insufficiency and stenosis. (*From Luisada and Liu. Am. J. Card.* 1958.)

EVALUATION OF PULMONARY HYPERTENSION. ulmonary vascular obstruction develops in a mall number of patients with predominant nitral insufficiency Similar to mitral stenosis, his may be important in prognosis, and evaluation may be advisable.

TRICUSPID VALVULAR DISEASE

Tricuspid valvular disease is of much less clinical significance than mitral stenosis because of its lower incidence and frequently the

Tricuspid Stenosis. Tricuspid stenosis is a rare lesion. It is usually associated with mitral valvular involvement and is usually accompanied by some degree of tricuspid insufficiency The major clinical findings which may suggest its presence are elevation of venous pressure and congestive visceromegaly In order to separate tricuspid stenosis from right heart failure per se, it is necesary to do a careful pullback of the catheter from the right ventricle to the right atrium, or else to employ a double-lumen catheter and to record a simultaneous beat-by-beat pressure gradient across the valve Not infrequently, the gradient is of only moderate magnitude and, particularly in the presence of chaotic atrial fibrillation, the detection of this gradient may be difficult. If a cardiac output and the diastolic filling period, measured on the right ventricular tracing, are measured along with the valvular gradient, then the appropriate hydraulic

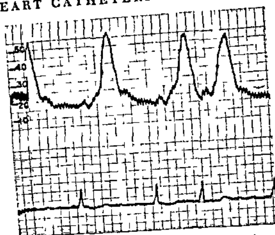


Fig. 7-46 Pulmonary capillary pressure pulse in pure mitral insufficiency (MI = 5 0 liters/min). This shows the peaked *C-V complex* and the plateau atrial diastolic pressure seen in pure mitral insufficiency.

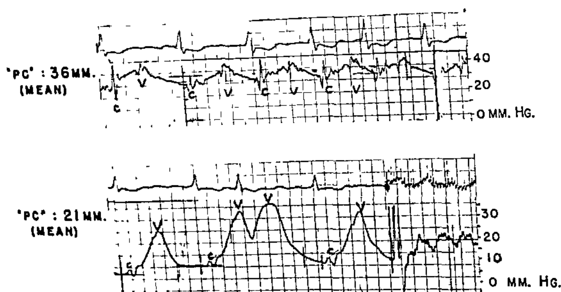


Fig. 7-45 Effect of valvuloplasty on pulmonary capillary pressure pulse with production of mitral insufficiency In the upper part of the figure is shown a pulmonary capillary pressure pulse in mitral stenosis. Note the wave characteristically seen in atrial fibrillation with a C and V wave with slow diastolic runoff after the V wave. In the lower half of the figure is shown the pressure tracing in the same patient after operative production of insufficiency. Note the lower mean pressure and the wider pulse pressure with the spiking V waves.

I

Right heart catheterization in rheumatic heart disease

RICHARD GORLIN

The introduction of the cardiac catheter as a clinical physiologic technique by Cournand and coworkers opened a new chapter in the understanding of valvular heart disease. In fact, only in 1946 Bloomfield and associates first demonstrated by right heart catheterization that the right ventricular pressure was elevated in patients with mitral stenosis, and at that time, they commented on the abnormal right atrial pressure pulse in tricuspid insufficiency. During the ensuing years, other workers demonstrated that the pulmonary arterial pressure and also the pulmonary "capillary" pressure were increased in mitral stenosis (Dexter et al). These observations were extended and a large number of publications added to the literature, all contributing to an understanding of the basic pathologico-physiologic process present in the various valvular diseases of the heart.

MITRAL VALVULAR DISEASE

Mitral Stenosis. In mitral stenosis, there are three problems to be assessed physiologically, viz., the degree of valvular stenosis, the height of pulmonary arteriolar resistance, and the presence and severity of right heart failure

DEGREE OF VALVULAR STENOSIS. Correlation of physiologic observations with clinical findings permits *clinical* evaluation of the degree of anatomic mitral stenosis in approximately 85 per cent of patients in whom the lesion is pure. The presence, type, and degree of symptoms, physical signs, x-ray silhouette, and electrocardiographic findings usually indicate accurately the severity of the mitral stenosis. In the remaining 15 per cent of patients, such accurate assessment is not possible. This is usually due to inadequate history, conflicting findings by various clinical methods, or the presence of multiple valvular lesions. In general, left heart catheterization is the procedure of choice because the direct valve pressure gradient may be measured. Prior to the widespread use of this procedure, right heart catheterization was useful, and still is if the technique of left heart catheterization is not available. When the valve pressure gradient is small, it is advisable to elicit an increase in this gradient by *exercise*. It is usually not feasible to carry out standard effort using the left heart technique, unless rather elaborate preparations are made. Therefore, if the transvalvular pressure gradient, measured during left heart catheterization, has been equivocal, such as may occur with chaotic atrial fibrillation and low cardiac output, standard exercise should be performed during right heart catheterization.

To make the necessary observations, the catheter is wedged into the pulmonary artery as far as it will go. The pressure recorded from the occluded pulmonary artery is a reflection of pulmonary venous pressure. Both mean and phasic pressures can be obtained successfully in over 85 per cent of patients. It may be difficult to obtain this pressure in patients with markedly elevated pulmonary vascular

EVALUATION OF PULMONARY HYPERTENSION. Pulmonary vascular obstruction develops in a small number of patients with predominant mitral insufficiency. Similar to mitral stenosis, this may be important in prognosis, and evaluation may be advisable.

TRICUSPID VALVULAR DISEASE

Tricuspid valvular disease is of much less clinical significance than mitral stenosis because of its lower incidence and frequently the secondary nature of that involvement. In occasional cases, however, intrinsic disease of this valve may be of importance. It is readily accessible to study by right heart catheterization.

Tricuspid Stenosis. Tricuspid stenosis is a rare lesion. It is usually associated with mitral valvular involvement and is usually accompanied by some degree of tricuspid insufficiency. The major clinical findings which may suggest its presence are elevation of venous pressure and congestive visceromegaly. In order to separate tricuspid stenosis from right heart failure per se, it is necesary to do a careful pullback of the catheter from the right ventricle to the right atrium, or else to employ a double-lumen catheter and to record a simultaneous beat-by-beat pressure gradient across the valve. Not infrequently, the gradient is of only moderate magnitude and, particularly in the presence of chaotic atrial fibrillation, the detection of this gradient may be difficult. If a cardiac output and the diastolic filling period, measured on the right ventricular tracing, are measured along with the valvular gradient, then the appropriate hydraulic

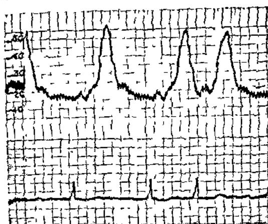


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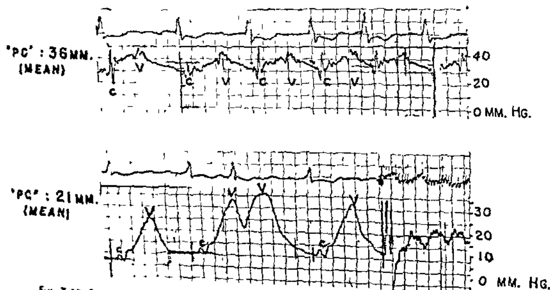


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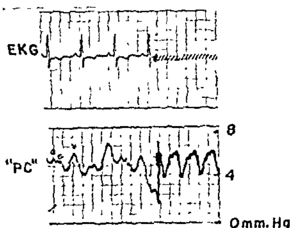


Fig. 7-44. Pulmonary "capillary" pressure pulse with simultaneous ECG in a case of pulmonic stenosis. Note the normal a, c, v wave pattern corresponding to atrial systole, valve closure, and atrial filling, respectively.

method while the catheter is in the pulmonary artery. These values may then be placed into the standard resistance formulas and the resistance expressed either in "R" units or in dynes-seconds-centimeter^{-5}. The second system has arbitrarily been used in the author's laboratory Normal values range up to 150 and up to 300 in patients with primary valvular stenosis. In the presence of pulmonary vascular disease, the values may run anywhere from 300 to 2,000 dynes/sec/cm^{-5}.

DEGREE OF HEART FAILURE. The presence of right heart failure in mitral stenosis is usually obvious. The venous pressure is generally elevated, and there is evidence to suggest a low cardiac output. However, both elevated venous pressure and low cardiac output may stem from causes other than right heart failure Finding an *elevated diastolic pressure* within the right ventricle confirms failure and, if equal to right atrial pressure, excludes tricuspid stenosis as a cause of the venous pressure elevation It is necessary to know the cause of the right heart failure. If failure is present and the pulmonary arterial mean pressure is 50 mm Hg or more (whether due to valvular or vascular obstruction), then the heart failure has come about (at least in part) as a result of an increased work load against pressure and should improve with valvuloplasty. On the other hand, if pulmonary arterial pressure is not found to be elevated, yet right heart failure is present, then it is due primarily to myocardial disease. These factors are easily assessed during right heart catheterization by measurement of right ventricular diastolic and right atrial mean pressures during withdrawal of the catheter from the pulmonary artery.

MITRAL INSUFFICIENCY. Assessment of mitral insufficiency by any catheterization technique is unsatisfactory at present. If the procedure is the only one used in the laboratory, right heart catheterization can play a minor role Information of three types may be obtained

PULMONARY WEDGE PRESSURE PULSE. The pulmonary wedge pressure usually gives a reasonable reflection of the left atrial pressure wave form (Fig. 7-44). In mitral insufficiency, the C wave[1] is increased, the X wave (the descent of the base) is frequently obliterated, and the V wave is unusually high,[2] with a large fall to atrial diastole (Figs. 7-45 and 7-46). This pressure pattern unfortunately is not diagnostic because it is influenced by the volume-pressure characteristics of the venoatrial bed, the degree of congestion of this bed, the cardiac rhythm, and the cardiac output. However, when the pressure pulse *shows a marked* phasic swing (Figs. 7-45 and 7-46), one can be sure that mitral insufficiency constitutes part if not all of the problem. It should be emphasized that only a qualitative interpretation of these curves may be made

ESTIMATION OF REGURGITATION BY DILUTION CURVES. *Korner and Shillingford* have recently analyzed the dye-dilution curves and shown that mitral insufficiency may be detected from variations in the slope of these curves. This is based primarily on the volume of residual blood between the point of injection and the point of sampling Usually this volume is increased in mitral insufficiency and, therefore, the diagnosis of mitral insufficiency can be made. It is not germane to this discussion to describe the method of analysis.[3] Suffice it to say, those who are interested in indicator-dilution-curve analysis in mitral insufficiency may best perform the maneuver by injecting the indicator into the wedged pulmonary artery catheter with sampling downstream, preferably from a brachial artery, through a standardized collection system.

[1] This wave is called AV wave by Luisada and Liu *Editor.*

[2] For interpretation of this wave, see also next chapter *Editor.*

[3] See Part 4, Chap. 6. *Editor.*

at rest and again after a similar period of standard exercise. Change in left ventricular systolic pressure may be estimated, as described elsewhere, and a calculation of cardiac work is carried out. Fixation of stroke work with rise in pulmonary wedge pressure constitutes circumstantial evidence of severe aortic stenosis.

Another finding, which is characteristic of severe aortic stenosis, is *fixation of coronary blood flow*. Coronary blood flow was measured by the *method of Kety and Schmidt*, at rest and after administration of nitroglycerin. Normally, flow increases 60 per cent and coronary resistance decreases 45 per cent In tight aortic stenosis, the coronary flow and coronary vascular resistance show little change after nitroglycerin Similar findings have been made in coronary artery disease In patients with aortic stenosis, who do not have a markedly increased left ventricular work load and who are not in end-stage heart failure, coronary blood flow can increase as in normal individuals Thus, a study of the coronary circulation by coronary venous catheterization may afford interesting, although indirect, evidence concerning the severity of the aortic valvular lesion

A characteristic sign of aortic stenosis may be seen in the pulmonary wedge pressure pulse The A wave of atrial systole is frequently increased. Rarely in aortic stenosis with heart failure, pulmonary vascular resistance may be increased This is hardly ever a severe enough degree to present as a clinical problem except when terminal heart failure ensues.

Aortic Insufficiency. Except for the academic interest of studying the work or filling pressure response of the left ventricle during exercise, right heart catheterization has little or no role in the study of aortic valvular insufficiency. The *Korner-Shillingford method* of indicator-dilution analysis may give erroneous values in aortic insufficiency and hence should be used with caution during right heart catheterization.

SUMMARY

Right heart catheterization was important in the early understanding of mitral, tricuspid, and aortic valvular disease. Because the mitral and aortic valves are on the left side of the heart, their quantitative analysis is best done by left heart catheterization. However, in mitral stenosis, where the degree of pulmonary vascular obstruction and the cause of right heart failure may be serious problems, actually dominating the clinical picture over the valvular obstruction, right heart catheterization may offer valuable information. In tricuspid stenosis, the diagnosis undoubtedly may be made only by right heart catheterization. Some of the hemodynamic consequences related to valve hydraulics and heart work in aortic stenosis are again best studied by right heart catheterization

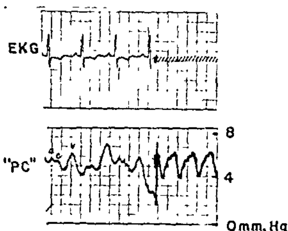


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normal limits, increase in pressure is not linearly correlated with the increase of atrial volume. The authors have studied the border tracing of the left atrium by electrokymography (left atrial volume curve) and the left atrial pressure pulse in the same patients and found that their patterns are usually similar. Unfortunately, the EKy of the atrium cannot give at present the exact value of changes of atrial volume. The expansion caused by regurgitation occurs under a high ventricular systolic pressure It is a pressure-volume-pressure change which cannot be determined as yet. The systolic elevation (insufficiency wave) above the diastolic pressure level may not increase in a linear fashion in regard to the volume of regurgitant blood. The level of *mean atrial pressure* during ventricular systole gives a more reliable evaluation of the regurgitation than the absolute value of the regurgitant wave The *absolute height* of the regurgitant wave should not be entirely attributed to the result of insufficiency unless stenosis of the AV valve or resistance to flow (as in myocardial fibrosis or constrictive pericarditis, etc) can be ruled out. In the presence of stenosis, only the *difference in level* between systole and diastole (mean systolic elevation) should be taken into consideration

AORTIC VALVE. A low diastolic pressure and a wide pulse pressure are usually accepted as evidence of aortic regurgitation in syphilitic or rheumatic heart disease However, it is not uncommon to find both a normal diastolic and a normal pulse pressure in adults with clinical evidence of aortic insufficiency and stenosis Intracardiac phonocardiograms taken in the ventricle or the aorta near the valve may give certain information because a diastolic murmur is usually present in cases with insufficiency Still, the insufficiency of the semilunar valves is more difficult to evaluate than that of the AV valves from pressure tracings, except in severe cases.

ABNORMAL PRESSURE MEASUREMENTS AND THEIR INTERPRETATION

Aortic Stenosis. Impressive results are obtained by recording *simultaneous pressure tracings* of the aorta and left ventricle, with the same calibration and the same zero reference line. As an alternative, a pressure tracing can be recorded while making a *pullback maneuver* across the aortic valve. A pressure tracing during a pullback across a stenotic valve guarantees the same sensitivity of pressure transducer, amplifier, and recording system and the same zero reference line

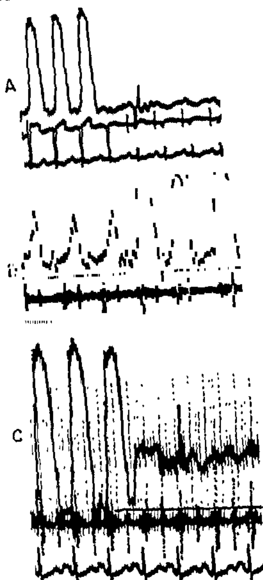


Fig. 7-48. Left ventricular and atrial pressures obtained by pullback and push-forward maneuvers. A. Normal mitral valve (pullback). B. Mitral insufficiency (push forward) C. Mitral stenosis and minimal insufficiency (pullback).

It should be kept in mind that a pullback pressure tracing across a semilunar valve cannot detect a dynamically insignificant stenosis.

For example, no systolic gradient of pressure between the aorta and left ventricle was found at rest in a patient with a systolic grade III mur-



Fig. 7-47. Normal right atrial pressure pulse. The three waves per beat: A, C and V are illustrated with a marked negative wave between A and C

formula may be utilized to calculate the anatomic area of the tricuspid valve

Rarely, the patient with tricuspid stenosis has a normal sinus rhythm. In this event, a nonspecific but suggestive clue to the diagnosis may be obtained from the jugular or right atrial pressure pulse. This will show an *unusually large A wave of atrial contraction*

Tricuspid Insufficiency. Tricuspid insufficiency is a very common lesion. In most instances, the valvular insufficiency is dependent upon dilatation of the right ventricle and the AV ring secondary to heart failure Insufficiency not infrequently occurs in association with tricuspid stenosis, in which valve closure is limited by thickening, shortening, and fusion of the leaflets Organic tricuspid insufficiency as an isolated lesion due to rheumatic valvulitis occurs only rarely

This lesion is best detected from the right atrial pressure pulse or its reflection in the jugular vein. In contrast to the normal (Fig 7-47), the pressure pattern shows again a large C wave,[4] a loss of the X wave, and a large climbing V wave.[5] The interpretation of this finding is, of course, limited by the presence of atrial fibrillation, which can affect the pressure pulse similarly. In addition, the quantitative aspects of the curve are affected by the venous-atrial volume elasticity characteristics, the degree of distention of this system, and the net cardiac output.

In a fashion similar to mitral insufficiency, a *Korner-Shillingford analysis* of the indicator-dilution curves may be applied to the study of the tricuspid valve. By injection of indicator, first into the superior vena cava and then into the pulmonary artery with brachial artery sampling after each injection, it is possible by study of the two curves to localize and quantitate the degree of tricuspid insufficiency. In actual clinical practice, however, this is of little importance. The magnitude of the lesion can frequently be judged best clinically by observation of the venous pulse, the activity of the right ventricle, and the expansion of the liver with systole.

AORTIC VALVULAR DISEASE

Aortic Stenosis. In aortic stenosis, left heart catheterization is the procedure of choice. There are, however, two aspects of the hemodynamics of aortic stenosis which may be studied by right heart catheterization The first of them is the response of the heart to standard effort. It has been shown that the stroke work of the ventricle is fixed if the aortic valve area is much less than 0.7 cm^2. While this finding is not specific for aortic stenosis, it may be helpful in individual cases to determine if stenosis is severe. In addition, the presence of borderline left heart failure may be detected by observation of the pulmonary wedge pressure at rest and then upon effort *In tight aortic stenosis, this pressure, even if normal at rest, rises precipitously on effort*

In order to elicit these findings, the right heart catheter is wedged in an end pulmonary artery, pressure is measured at rest and at the end of a standard period of exercise—usually 3 min—at which time this pressure level is stable The catheter is then withdrawn to the pulmonary artery, the needle inserted into the brachial artery, and observations of brachial arterial pressure and cardiac output are made

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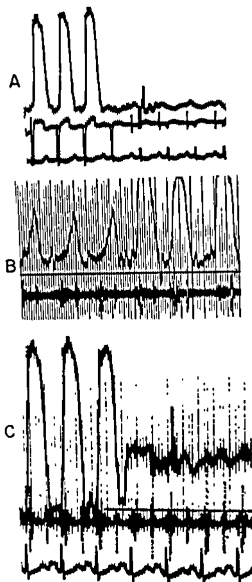


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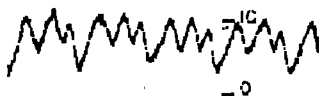


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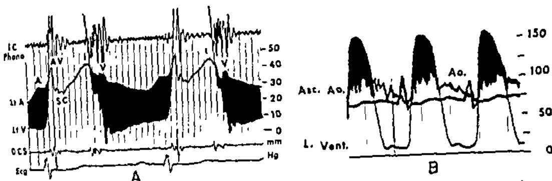


Fig. 7-50. A. Simultaneous left atrial and left ventricular pressures in a case of mitral stenosis (diastolic gradient) and minimal insufficiency (I wave in late systole). B. Simultaneous aortic and left ventricular pressures (systolic gradient).

be considered as conservative because a perfectly normal mitral valve shows *no* gradient (Fig 7-48A) However, it should be kept in mind that any existing gradient would be increased by greater venous return, and usually exercise increases the gradient For this reason, an *exercise test* should be made in doubtful cases

The pressure gradient across the mitral valve can vary from 5 to 30 mm Hg As pulmonary edema develops when the pulmonary capillary pressure is above 32 mm Hg for any length of time (Fleury), the diastolic pressure of the left atrium seldom rises above 30 in basal conditions Paroxysmal rises are, of course, possible

Mitral Regurgitation with or without Stenosis. A high *systolic insufficiency wave* (I wave or I–V wave)[1] in a direct left atrial pressure measurement has been described as the result of mitral regurgitation (Fig 7-48B) However, any proportion between the height of the systolic I wave or I–V wave and the severity of mitral regurgitation has been denied by others Several methods of study of the left atrial pressure pulse have been described in order to distinguish the pattern of significant mitral insufficiency from that of mitral stenosis However, because of a nonlinear increase of the pressure of the left atrium whenever there is an increase of left atrial volume due to a regurgitant jet, an exact evaluation of the severity of mitral regurgitation in the presence of predominant stenosis is still impossible.

Left atrial mean pressure should be measured during ventricular systole by planimetric integration between the AV and the V waves (for 10 consecutive systoles or systoles in one or more respiratory cycles). The heart sounds recorded by a phonocardiogram are excellent for timing the opening of the mitral valve. Diastolic pressure of the left atrium and ventricle has been described previously.[2] A mean elevation of the left atrial pressure during ventricular systole above 3 mm Hg over the atrial diastolic pressure indicates mitral insufficiency The square root of this elevation is termed the *insufficiency index.*

In the presence of severe mitral stenosis with a stenosis index above 3.16, the insufficiency index (square root of the systolic elevation of the mean left atrial pressure above atrial diastolic pressure) cannot be correlated with the amount of regurgitation because the atrial wall is continuously kept under great tension On the other hand, a slight increase of mean left atrial pressure during ventricular systole usually indicates a significant mitral regurgitation if the stenosis index is below 3 16

The left atrial pressure pulses, analyzed by the method of Owen and Wood, modified by Morrow et al, is useful in order to select patients with pure or predominant stenosis According to Owen and Wood, P_1 = pressure of I-V waves, P_2 = y descent, T_2 to T_1 = time in seconds from P_1 to P_2, Ry ratio = $P_1 - P_2/T_2 - T_1$ mm Hg/sec. Index of Owen and Wood = Ry/P_1 ratio. Index of Morrow et al = Ry/La mean However, in the presence of severe mitral stenosis, the value of this index for the detection of significant regurgitation is open to question.

[1] This wave has been called "V wave" by several authors As pointed out by us, the peak of this wave occurs, in the majority of cases, prior to or coinciding with the 2d aortic sound Therefore, it is a new pathologic wave Occasionally, it may be prolonged into protodiastole and fuse with the V wave.

[2] See Part 4, Chap. 12, also Table 7-9. *Editor.*

1

Left heart catheterization in rheumatic heart disease

ALDO A. LUISADA AND CHI KONG LIU

GENERAL CRITERIA OF INTERPRETATION OF A *PRESSURE TRACING*

Evidence of Dynamically Significant Valvular Stenosis. When the functional area of a valve is reduced to a critical level, valvular resistance to blood flow at rest occurs. The pressure behind the stenotic valve increases in order to maintain a normal (or slightly reduced) flow. Therefore, a *systolic pressure gradient* develops across a narrow *aortic valve* and a *diastolic pressure gradient* develops across a narrow *mitral valve* Since the square root of a pressure gradient is directly related to the amount of flow and inversely related to the size of the opening, both the pressure gradient and the flow across the valve are important in order to evaluate the functional orifice of a stenotic valve Unfortunately, in rheumatic mitral or aortic stenosis, a certain degree of concomitant insufficiency is frequently present. The forward flow across the valve, obtained by Fick's principle, does not include the backward flow due to the insufficiency.

The estimation of a regurgitant flow cannot be calculated unless actual measurement of the valvular area has been done at autopsy or surgery. Neither of them is obviously available for preoperative evaluation. Although an indicator-dilution curve is claimed to be of value for the calculation of regurgitation, its accuracy needs further proof. With the existence of this unknown factor, it is apparent that the *pressure gradient* across a valve indicates only a dynamically significant degree of stenosis, while the absolute value of the latter can be calculated only on the basis of the actual forward flow. On the other hand, if no evidence of regurgitation is revealed by the pressure-pulse pattern, as well as by clinical examination and other laboratory data, the greater the pressure gradient, the smaller is the valve, provided that cardiac output at rest is normal or only slightly reduced. The authors wish to emphasize further that the functional area of a stenotic valve should be correlated with the weight or body-surface area of the patient.

Evidence of Dynamically Significant Valvular Insufficiency. MITRAL VALVE. Theoretically, a systolic elevation of atrial pressure should be considered evidence of regurgitation through the incompetent valve because regurgitation into the atrium occurs under a high ventricular systolic pressure. In normal subjects, left atrial mean pressure during ventricular systole is not higher than the pressure at mid- or late diastole. The characteristics of either normal or abnormal human atrial distensibility are unknown.

In normal dogs, volume-pressure changes of [illegible]

[illegible] its of *pressure are passed*, a slight increase in *volume* causes a great increase in pressure In other words, when atrial pressure exceeds the

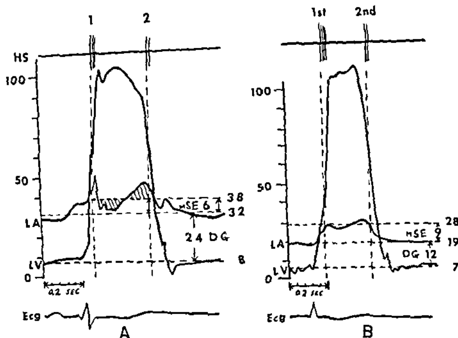


Fig 7-52 A. Left ventricular (LV) and *left atrial (LA) pressure tracings* in a case of severe mitral *stenosis with minimal insufficiency*. B. Left ventricular and left atrial pressure tracings in a case of moderate mitral stenosis and moderate mitral insufficiency SE, systolic elevation; DG, diastolic gradient; HS, heart sounds. (From original tracings)

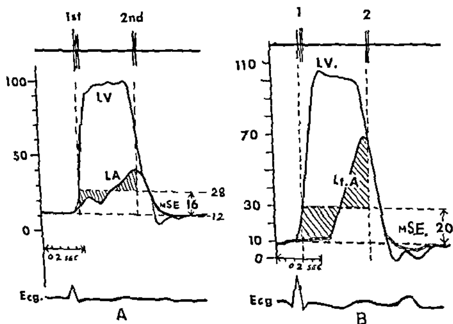


Fig 7-53 A Left ventricular and left atrial pressure tracings in a case of medium-severe *mitral insufficiency* with no stenosis. B Left ventricular and left atrial pressure tracings in a case of extremely severe *mitral insufficiency* and no stenosis Symbols as in Fig. 7-52 (From original tracings)

mur over the aortic area. The patient died 8 months later. At autopsy, the aortic leaflets were fused and calcified, forming a triangular orifice estimated to have an area of 0.9 cm^2. When a semilunar valvular orifice is reduced to a smaller area (0.6 cm^2), then ventricular systolic pressure becomes higher than that of its respective great vessel.

Since the calculation of the functional valvular area of a narrowed valve requires mean systolic pressure difference, the pressure measurement of mean systolic pressure of the ventricle and aorta is important. *Mean systolic pressure of the aorta* is measured from the beginning of the upstroke to the dicrotic notch. Likewise, *mean systolic pressure of the ventricle* is measured from the point where the pressure just exceeds that of the artery to the highest point. This measurement should include several systoles in one or more respiratory cycles or in 10 consecutive beats (patients with atrial fibrillation) The pressure gradient across the aortic valve may be moderate or may reach extremely high values, even 100 mm Hg or more (Fig. 7-49B).

The square root of the mean systolic pressure gradient, which is proportional to the degree of narrowing of a stenotic orifice, is termed the *stenosis index*

In aortic stenosis, the authors usually advise aortic valvotomy when a patient of middle age has a stenosis index greater than 7 with repeated episodes of left heart failure The authors would like to emphasize that clinical judgment is as important as the magnitude of the stenosis index and the calculated functional valvular areas. On the other hand, clinical judgment alone is frequently inadequate if not correlated with technical data.

Aortic Insufficiency. In severe aortic insufficiency, aortic diastolic pressure is usually below 40 mm Hg, but in many cases this has not been verified by pressure tracing.

Mitral Stenosis and Insufficiency. The necessary requirements for a correct evaluation are: (1) patient at rest; (2) evaluation during one (or possibly more) pullback maneuvers, thus obtaining the same conditions and degree of amplification; (3) measurement of the diastolic pressure both in the atrium and ventricle at mid-diastole (if there is atrial fibrillation) or just prior to the atrial contraction (in cases with sinus rhythm), (4) average of at least 10 cycles for the atrium and the ventricle during normal respiration. (See also Part 4, Chap. 12.)

In cases with sinus rhythm, the *highest point prior to the presystolic A wave* (0.14 sec before the Q wave of the ECG) should be accepted as the reference level In cases with atrial fibrillation, while diastolic atrial pressure may be high during short diastoles, long diastoles often allow the pressure to drop gradually to near normal levels. For this reason, the pressure measured at about one-half of diastole (average of 10 similar cycles) should be accepted as the actual diastolic level of atrial pressure.

Dynamically significant mitral stenosis should be admitted when a gradient of more than 5 mm Hg is found between the diastolic pressure of the left ventricle and that of the left atrium (Fig. 7-48C). Even this limit should



Fig. 7-49. Aortic, left ventricular, and left atrial pressures obtained during a continuous pullback from the aorta to the left atrium. Normal aortic valve, mitral stenosis, slight mitral insufficiency.

14

Surgery of mitral stenosis

DWIGHT E. HARKEN AND WARREN J. TAYLOR

Samways (1898) first suggested slight notching of the mitral orifice with the hope of creating insufficiency. This, he thought, would be better tolerated by the patient "*assuming* the auricle would continue its *defense*." Lauder Brunton (1902) carried out experimental work on autopsy specimens with the view *toward converting* stenosis into insufficiency. MacCallum, Cushing, Branch, and Bernheim (1907 to 1909) at Johns Hopkins experimented with the conversion of stenotic into insufficient valves. Allen and Graham (1922) developed a cardioscope with a convex lens at its end which brought into view surfaces where blood was displaced by *contact*. The lens was grooved in the middle of its convex contact surface to carry an L-shaped knife that worked as a hook guillotine. Graham tried to use this instrument on human beings. The brave but disappointing adventures of Cutler, Levine, and Beck took place in the Peter Bent Brigham Hospital (1923 to 1927). They hoped to create insufficiency by punch valvulectomy of the major (aortic) leaflet through a ventriculotomy. Their initial patient, an 11-year-old girl, survived for 4½ years. Six more patients were operated, but all succumbed. Cutler, Levine, and Beck developed "an operating cardioscope," but those who have used these and its clear plastic displacement balloon was remarkable, more for what one could *not rather than* for what one could *see*.

Two years after Cutler's initial success, Souttar carried out a successful "dilatation of the mitral valve" by introducing his index finger through the auricle. Bourne (1927) suggested that an extension of the "mitral slit" at its extremities might be preferable to one made laterally in the cusp.

Bailey (1945) revived the concept of converting stenosis into insufficiency. His first patient died of hemorrhage from a torn atrium. A year later, again with the thought of accepting insufficiency to correct stenosis, he operated again. Unable to pass an instrument *through the* valve and recalling Souttar's report, he inserted his finger through the auricle and split the anterior and posterior commissures. Unfortunately, this patient succumbed 24 hr later. Autopsy confirmed the commissural spits and considerable restoration of leaflet mobility.

In the meantime, Harken was attacking the problem from various *directions*. Four patients were operated. Accepting the thesis that patients with Lutembacher's syndrome fared better than those with mitral stenosis alone, *Harken surgically* created *interatrial* septal defects in two patients with stenosis. Both patients survived, but improvement was neither impressive nor prolonged.

On the basis of a previous experience ("selective insufficiency") which demonstrated *that tachycardia* was poorly tolerated by patients with mitral stenosis, a third patient underwent sympathetic denervation. Improvement of the patient was transient, and such efforts were abandoned. A fourth patient had a direct valvular operation.

Thus far, the underlying thesis for direct valvular surgery had been the *erroneous concept that insufficiency was better tolerated than stenosis*. Furthermore, there was no appreciation of the different functions of the major (aortic) leaflet, versus the *minor* (ventricular) leaflet. In 1940 to 1942, Harken had resected *various* areas of the leaflets and found that valvulectomy involving the major (aortic) leaflet was not tolerated. Contrariwise, valvulectomy of similar areas in *the* ventricular leaflet did not seem to interfere as much with valve action. Further studies of valve function indicated that the major leaflet moves *in systole so* that it not only contributes to closure of the mitral orifice but directs blood toward the aorta. It acts as one wall of a cylinder at the top of

TABLE 7-9. PRESSURES OF THE LEFT HEART IN PATIENTS WITH NORMAL MITRAL VALVE AND NO EVIDENCE OF LEFT VENTRICULAR FAILURE

No.	Age, years	Left atrium							Left ventricle	
		a	av	S C.	v	Mean systole	Diastole	Mean	Systole	Late diastole
1	32	12.6	14.7	3.7	10	7.0	6.9	8 3	148	7 0
2	36	8	7.0	4	7	5.8	6.2	6.0	97	6.2
3	38	15	12 5	6	10	8.0	9 0	9.5	100	8-9
4	40	13		4	5	5 0	6.0	7.0	95	6
5	37	12	6.8	4.6	8.7	7.0	7.4	7.6	112	7.4
Average		12 1	8.2	4.5	8.2	6.6	7.1	7.7	110	7 0

The height of the triangular wave of insufficiency may reach even 70 mm Hg. This pressure would be incompatible with life if sustained. Actually, in our cases, the *mean* atrial pressure was never higher than 30 to 32 mm Hg.

PATTERNS OF PRESSURE

Left Atrial Tracings. The authors have studied this type of tracings in 22 cases through left heart catheterization (Table 7-9). Decision of the type of hemodynamic disturbance was based on the diastolic gradient and the systolic elevation

EVIDENCE OF MITRAL STENOSIS The hemodynamic diagnosis of mitral stenosis is based on the determination of a diastolic gradient across the mitral valve.

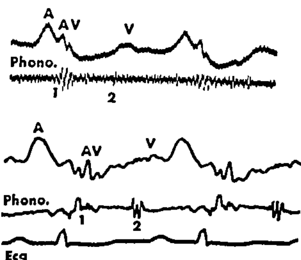


Fig. 7-51. Pressure tracings of the left atrium in two cases with normal mitral valves.

EVIDENCE OF MITRAL REGURGITATION. Considerable confusion exists in the literature in regard to the evidence for mitral regurgitation. The left atrial pressure tracing of *normal individuals* (five cases observed by the authors) shows a gentle depression during ventricular systole, between *AV* and *V* (Fig 7-51). As this is due to lowering of the AV floor by left ventricular pull, it is possible that rigidity of the mitral leaflets decreases this depression, but it is unlikely that it may prevent it or, even less, reverse this motion

It has been said that, in patients with severe mitral stenosis, filling of the left atrium during systole from the pulmonary veins (which have a very high pressure) is so rapid that it simulates the pattern of mitral regurgitation. However, this would account for only a minimal rise of mean pressure (3 mm Hg) above the late diastolic pressure during ventricular systole because the pulmonary veins cannot act as a pump On the other hand, whenever a diastolic pressure gradient across the mitral valve is absent or minimal, and there is a significant rise of mean pressure during ventricular systole (3 mm Hg or more), it is apparent that blood flowing into the atrium must come from a high blood pressure chamber, i.e , the left ventricle. *If the pattern of the pulse in the atrium resembles that of the ventricle, then no other possibility can be accepted.*

As various patterns can be found in mitral patients, the authors decided to evaluate any *systolic elevation of pressure* in millimeters by using a planimetric method. It is obvious that,

funnel (type II) (*Fig.* 7-55B) The stenotic orifice may face the ventricular wall (group A) or the outflow trace (group B) (Fig. 7-56).

Figure 7-55A, showing pathologic process type I, illustrates the fact that bridges of fusion between the major and minor leaflets constitute a rigid zone that is in continuity with a similar rigid marginal zone around the lips of the stenotic orifice There may or may not be calcific deposits in these fused and rigid areas. The chordae tendineae and papillary muscles may be essentially normal and continue to perform their functions as moorings for the parachute-like leaflets. The major (aortic) leaflet is intact and is usually flexible in its peripheral two-thirds If the anterior and posterior fusion bridges are broken, the leaflets are then released to swing freely. Both opening and closure are improved Thus, valvuloplasty can correct stenosis and may correct minor degrees of regurgitation Type I mitral stenosis is the form seen in the majority of patients studied at operation and at autopsy

In the illustration of pathologic type II (Fig 7-55B), a different fusion bridge is encountered Here uniform fusion presents an elastic funnel formation with extension of the process to the chordae tendineae The chordae are shortened, thickened, and fused and may even form a secondary obstruction This does not lend itself well to simple "finger-fracture valvuloplasty." Incisional valvuloplasty with valvulotomes such as those developed by Bailey, Harken, Brock, O'Neil, and others may be useful in this situation. It cannot be overemphasized that increased experience and greater patience will make "impossible" or "inoperable valves" only relative terms. Great care and the skullful use of fracturing force with the finger and incision with the right knife make essentially all stenotic orifices correctible. The surgeon may need to change position, even cross to the opposite side of the table, to deliver just the proper fracturing force, but it can generally be accomplished.

Stenosis of either type I or type II may carry orifices of similar size yet be associated with different degrees of regurgitation, depending upon the direction that the mitral opening faces. If the funnel is turned toward the ventricular wall, the opening may be closed in systole by the myocardium and thus prevent regurgitation. If the mitral orifice points into the outflow tract, it may scoop blood in systole, with resultant regurgitation. *Stenosis without regurgitation is called group* A and that *associated with regurgitation, group B* (Fig 7-56). It is immediately apparent that any one patient may present any variation of the pathologic process in the spectrum

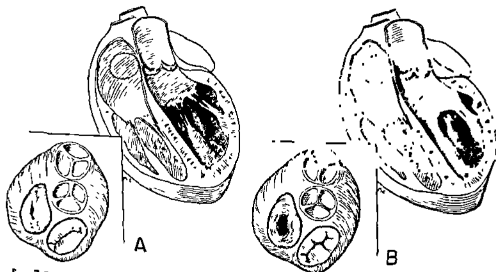


Fig 7-55 A Type I *mitral stenosis* A common pattern of mitral stenosis with (a) marginal leaflet fusion and calcification, (b) leaflet flexibility remaining, (c) only minor thickening and fusion of chordae tendineae, (d) right ventricular and pulmonary artery enlargement This may be of group A or B B Type II mitral stenosis A less common but not unusual form of mitral stenosis witht (a) flexible funnel fusion of leaflets, (b) fusion of chordae tendineae, (c) no calcification, (d) enlargement of right ventricle and pulmonary artery This may be of group A or B.

in the case of a flat plateau (Fig. 7-52B), the center of the latter coincides with the line of mean elevation, while in the case of *a triangular wave* bisecting systole, the line of mean elevation would be at about halfway from the top (Fig. 7-53B). It was also decided to accept this *mean systolic elevation* as an approximate measure of mitral regurgitation (see previous "criteria").

The study of the pressure pattern of the left atrium revealed the following typical configurations:

1. Several cases of *pure mitral stenosis* were observed. In all of them either there was *a high A wave* (sinus rhythm) (Figs. 7-50 and 7-52A) or the pattern was normal.

2. Five cases of *pure mitral insufficiency* were studied. They presented a triangular *late systolic wave (I wave or "insufficiency wave")*, which only occasionally fused with the following (early diastolic) V wave (Figs. 7-48B and 7-53B).

3. Eleven cases of *mitral stenosis plus insufficiency* were observed. They usually showed a new pattern which consisted of a *plateau-like wave* during ventricular systole Three variations of this pattern were found:

a An AV notch followed by a drop which, however, failed to reach the diastolic level This was called an "intermediate pattern" and interpreted as evidence of *minimal insufficiency* in the presence of severe stenosis.

b. A large A wave, partly fused with the AV notch. then followed by a drop which did not reach the diastolic level (Fig. 7-52A) This was considered evidence of *moderate insufficiency in the presence of stenosis.*

c. With either sinus rhythm or atrial fibrillation, there was *a plateau-like wave* during ventricular systole (Fig. 7-52B). This showed either a flat top or an oblique rising line. The end of the plateau was before, at, or after the 2d sound. This pattern was interpreted as evidence of *moderate insufficiency in the presence of moderate to severe stenosis.* The drop of pressure at the end of the plateau started *before* the 2d sound when left atrial pressure was very high, *at* the 2d sound in the average cases, and *at the time of the V wave* in the few cases with minimal stenosis. Thus, the end of the plateau behaved either like an *I* or an *I–V wave.*

The importance of left atrial pressure is revealed by cases with severe ventricular arrhythmia due to atrial fibrillation. In cycles preceded by a long diastole, where the left atrium empties well, the regurgitant pattern assumes a triangular aspect. On the contrary, in cycles preceded by a short diastole, where the left atrial pressure is higher (engorgement of the atrium), a better transmission of left ventricular pressure occurs, and a squarish plateau can be observed.

It is surprising that *pure insufficiency* should give a late systolic triangular wave while *insufficiency plus stenosis* should give a plateau-like pattern. One possible explanation is that in mitral stenosis, with its high atrial diastolic pressure, the atrial walls are kept under a state of persistent tension. Then, if regurgitation occurs, a more accurate reproduction of ventricular pressure takes place in the atrium. Still, it might be postulated that, during the first half of ejection, the musculature of the left ventricle tightens the mitral ring so much that it prevents regurgitation. This would explain why a typical squarish plateau is observed in cases of left ventricular failure and is more common with atrial fibrillation than without it (the AV sequence of contraction ensures a better closure of the mitral valve). It is likely that both explanations are correct.

larger than normal but small in relation to the large atrium, ventricle, and flow, produces the eddy currents of a loud diastolic murmur

When one visualizes the leaflet complex taut from distention in this dilated annulus, the mechanism of the diastolic murmur is easily understood. Some cardiologists, experienced in the selection of patients for surgery, have had their first clue of insufficiency in this sort of diastolic murmur. The systolic murmur associated with such a freely patulous mitral complex may be soft and almost inaudible. Conversely, if the mitral orifice is small, rigid, yet slightly patent in systole as in many forms of tight stenosis, the systolic murmur may be very loud. When very loud, it is of the high-pitch, high-velocity, low-volume variety. It seems entirely possible that some of these high-pitched murmurs may originate within the ventricle from eddy currents about the fused chordae and papillary muscles and not represent reflux at all. In some instances, a very low flow over a markedly stenotic orifice may produce no diastolic murmur. These dynamics are well demonstrated by the child's toy balloon When he blows it up and releases it, it darts about the room with air rushing out freely, making a low-pitch, high-volume fluffing sound. This is in sharp contrast to the loud, high-pitched, high-velocity, low-volume squeal emitted when the child stretches the neck of his balloon into a long slitlike orifice These situations can be related to the systolic phases of insufficiency and stenosis, respectively, wherein paradoxically, the systolic murmur of insufficiency may be less conspicuous than that in tight stenosis

Functional tricuspid insufficiency often complicates the late phases of mitral stenosis when the right ventricle fails This does not contraindicate mitral valvuloplasty Indeed, the right ventricle may regain its competent state after mitral valvuloplasty and correct this type of tricuspid insufficiency The clinical diagnosis of tricuspid *stenosis* is often made but rarely confirmed The "confirmation" at autopsy by finding peripheral fusion of the commissures must be interpreted as pathologic, not hemodynamic, stenosis The impression that 10 per cent of patients with mitral stenosis have organic and hemodynamically significant tricuspid stenosis is not consistent with our experience unless one includes the pathologic group just described and a group little appreciated—those having "functional tricuspid stenosis" Formerly, the diagnosis of tricuspid stenosis was made frequently. The diagnosis of tricuspid stenosis may be based on a marked diastolic gradient by catheter between the right atrium and ventricle Yet, at operation or autopsy, a freely patulous opening that would admit two or more fingers may be encountered. The peripheral commissural zones may be fused, but nothing hemodynamically significant can be felt or seen.

This paradox of auscultatory evidence of tricuspid stenosis with a diastolic murmur altered by respiration and heard over the tricuspid area, correlated with a gradient measured by catheter, yet palpated at operation to be 4 cm² or more in diameter, can be explained. Tricuspid stenosis, even minimal peripheral commissural fusion, is generally associated with mitral disease. This mitral disease, particularly stenosis, produces pulmonary hypertension, then right ventricular hypertrophy and even right ventricular failure and dilatation. Under the conditions of cardiac catheterization, the cardiac output and blood flow may be such that there is considerable elevation of the pulmonary artery pressure. This is of course sustained by the right ventricle, which may be dilated. If the anterior commissure of the tricuspid valve is partially closed, the tricuspid orifice may be dilated and distorted, so that what might in the flaccid state constitute an incompetent tricuspid valve complex, can be stretched into a slitlike orifice and become a real obstruction. Again recall the analogy of the child's balloon. Thus, when the ventricle is hypertensive and distended, there may be tricuspid stenosis ("functional"); yet uder low flow conditions of anesthesia at surgery, or in the flaccid state at autopsy, or after mitral stenosis has been corrected and pulmonary hypertension has receded, this functional tricuspid stenosis may disappear.

CLINICAL CLASSIFICATION OF PATIENTS WITH MITRAL STENOSIS

A *classification* based on surgical risk and eventual rehabilitation constitutes the background for selecting patients for surgery. Even though it is difficult to present an accurate and sound clinical classification suitable for selection of patients, the following working classification has been proved useful.

Group I comprises patients whose present course is *benign*. They have auscultatory signs of mitral stenosis but few, if any, symptoms and minimal evidence of increase in pulmonary vascular pressure. Patients in this group may continue to run a benign course or may develop an acceleration of their illness which shifts them to one of the other groups.

Group II includes patients *somewhat handicapped* by a static degree of moderate dyspnea on effort or by sporadic attacks of acute dyspnea or other pulmonary symptoms, provoked by unusual exertion, fatigue, or severe infection. They seldom have peripheral edema and

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of pulmonary edema or from peripheral or pulmonary infarction Their life expectancy under medical therapy is *hazardous*.

Group IV is a *terminal* group These patients are completely incapacitated, usually with right ventricular failure manifested by chronically elevated venous pressure, considerably enlarged liver, and a marked tendency to congestion. Their pulmonary disability may or may not be greater than those in group III They often have poor liver function, may have ascites, evidence of decreased peripheral blood flow, and many have had emboli. Most of them have atrial fibrillation

Certain additional factors of importance in evaluating patients for operation are not included in the above classification. These may jeopardize the good results from surgery but in themselves do not necessarily constitute contraindications.

Age over 50 does not significantly affect the results of valvuloplasty A review of 150 patients by Black and Ellis indicates that the results are comparable to those found in younger age groups "Age is a function of the proximity to the end of life not the distance from the beginning." A terminally ill patient in the younger age group may well be "older" than a well-preserved patient in his seventh decade Coexisting coronary insufficiency may be the cause of cardiac symptoms Differentiation may be complicated by absence of typical electrocardiographic evidence of right ventricle hypertrophy in this older group. However, in the presence of suspected significant stenosis, one should not hesitate to proceed with exploration. The results of operation have been gratifying.

Atrial fibrillation was once considered a "relative contraindication" It was present in 54 per cent of the authors' first thousand patients and in 84 per cent of those in group IV. Improved methods of managing atrial clots, including flushing and aspiration, have significantly reduced the danger of surgical emboli. It is unnecessary to attempt to revert a patient with atrial fibrillation to normal sinus rhythm in preparation for surgery. This is apparent if one considers two facts (1) Such a patient will almost certainly start fibrillating again after the atrial trauma represented by surgery (2) Danger of embolus from atrial thrombosis is probably greater on reversion before surgery than when the atrium is flushed at surgery. On the other hand, repeated emboli may indicate the need for an emergency *valvuloplasty*.

Coexistent mitral insufficiency[2] does not preclude valvuloplasty if stenosis predominates. Differentiation has been greatly clarified by increased clinical experience and by the additional information afforded by left heart catheterization and dye-dilution curves. Ellis's follow-up study of the authors' initial 1,000 valvuloplasties indicates that, in group III, there is similar improvement whether or not there was an associated mild insufficiency. When marked insufficiency was found, rehabilitation was less good but operation was generally worthwhile.

Calcification of the mitral valve increases the risk of surgery but does not constitute an absolute contraindication. Interruption of the cerebral circulation at the time when calcific particles may be dislodged from the valve tends to divert emboli to silent areas of the body.

Associated severe aortic disease in combination with mitral stenosis presents a challenging problem Where stenosis of both valves is suspected clinically, left heart catheterization may be invaluable (Fig. 7-58). If the associated aortic stenosis is significant, both aortic and mitral stenosis should be corrected *at one operation*

The *tricuspid valve* may be involved in certain cases. The nature of organic tricuspid stenosis or insufficiency is well appreciated. Functional tricuspid insufficiency associated with a failing right ventricle is also common and well known, functional tricuspid stenosis was previously discussed. In any event, when tricuspid involvement is suspected from clinical evaluation or after right heart catheterization, it is feasible to rotate the heart and approach the tricuspid valve through the right auricle If stenosis exists, it may be corrected. If the stenosis or insufficiency is "functional," proper mitral valvuloplasty should reduce pulmonary hypertension and bring about diminu-

[2] Mitral insufficiency, prior to or caused by operation, rheumatic fever, or technically unsatisfactory valvuloplasty are the commonest reasons for late deterioration An Ivalon operating tunnel has rendered this difficult and dangerous reoperation safe and clinically gratifying.

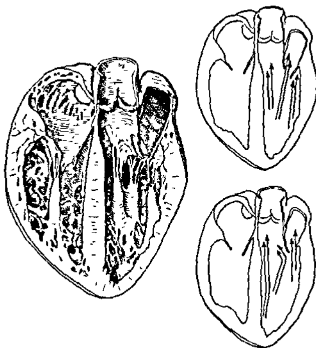


Fig. 7-54. Shunting, baffle, or "water-shed" function of leaflets The major or aortic leaflet must remain intact to act as a baffle to the aortic outflow tract. Defects in the lesser leaflet produce minimal regurgitation. Defects in the major leaflet produce marked regurgitation.

which is the aorta This concept of a shunting, or baffle, or water-shed function of the major leaflet is basic to successful correction of mitral stenosis. Fracture or incision of the aortic leaflet causes devastating regurgitation. Similar resection or incision of the ventricular leaflet corrects stenosis equally well, but does not compromise cardiac output to the same degree Furthermore, such a defect tends to close in systole This is the basis for the concept of "selective insufficiency" and warns against the very type of valvulectomy that earlier workers hoped to attain Had they been able to place their valvulotomes and excise a portion of the major leaflet as planned, their operations would in all probability have caused lethal regurgitation. This primitive concept of leaflet function is demonstrated in Fig 7-54

Appreciation of the dangers of regurgitation, and the goal of the best possible restoration of valve function, without the production of significant regurgitation, required a new descriptive word. The word *valvuloplasty* seemed to serve. It also indicated perhaps more completely than "commissurotomy" (introduced by Bailey the following year) that the maximal restoration of valve function would involve more than simply opening the fused commissures. Indeed the chordae tendineae and papillary muscles can so fuse in "secondary stenosis" that commissurotomy may be of no value.

In 1947, Harken attempted to create "selective insufficiency" by excising a portion of the ventricular leaflet. The procedure went well. Postoperatively, tachycardia developed. The patient died 24 hr later in pulmonary edema. Though this outcome was disastrous, it was the observation of this patient after surgery and at the autopsy table that clarified the mechanisms by which tachycardia is so poorly tolerated by patients with stenosis. It is appropriate to mention some of the factors. (1) The lungs and left atrium are decompressed of blood by forward flow through the mitral valve in diastole. The reduced mitral orifice makes this diastolic drainage time a critical factor. Tachycardia reduces the total diastolic time, therefore tends to dam blood back into the lungs (2) If there is associated regurgitation, each beat increases the total reflux jet, aggravating the pulmonary dam and congestion. (3) The right ventricle, if functioning effectively, pumps more blood into the lungs during tachycardia, further increasing the burden

The year 1948 ushered in successful surgical intervention by both Bailey and Harken. Both patients are alive 9 years later. In that same year, Brock revived the Souttar operation apparently without knowledge of the above work. Smithy (also independently) repeated Cutler's work by creating insufficiency with a transventricular punch. His patient survived. The ensuing years brought modifications of technique. Harken used the descriptive term "finger fracture" and added it to his word "valvuloplasty." This operation supplemented by various cutting instruments is basically the operation now in general use.

MORPHOLOGIC CLASSIFICATION OF MITRAL STENOSIS AND TECHNICAL CONSIDERATIONS IN VALVULOPLASTY

The clinical and pathologic manifestations of rheumatic fever are manifold. A clear understanding of the general morphologic types is fundamental to successful surgery.

Stenosis may exist as a *primary* form due to leaflet fusion or as a *secondary* form due to fusion of chordae tendineae and papillary muscles.

Primary stenosis may be due to commissural fusion (type I) (Fig. 7-55A) or may extend distally into the ventricle as an elastic

cedure, not a cure: the valve is not restored to normal, and other factors in the heart disease, not dependent on the mechanical obstruction, are not relieved.

Certain specific statements can be made. Group I patients are not accepted for surgery. In general, *group II patients* are not urged to have surgery. However, if their limitation is unacceptable to them, they are considered to be surgical candidates. This attitude is predicated on the extremely low operative risk and the substantial rehabilitation which they may expect. Group III patients are urged to have surgery. The operative risk is low (0.6 per cent), and rehabilitation is of the order of 80 per cent. Group IV patients have no alternative because they are in a terminal phase of their illness. The authors' control series of 19 patients who did not come to surgery emphasizes the validity of this statement: 17 of these patients died within 12 months, 15 of them within 6 months of the time surgical intervention was recommended. In patients of group IV, the operative mortality is high (20 per cent) and rehabilitation (60 per cent) significantly less. However, in view of the prognosis (as indicated by the control series), this high operative mortality is still acceptable when viewed as "salvage surgery."

The important lesson to be learned here is that the responsibility of the physician lies in the selection of his patient for operative intervention at a time when he is still properly classified in group III rather than in allowing him to progress into group IV, with its attendant increase in operative risk and decrease in rehabilitation. It is again emphasized that multiple lesions can be simultaneously corrected.

TOTAL SURGICAL MANAGEMENT

Successful surgery involves much more than a technical tour de force. The term "total surgical management" is used to embrace the proper selection of patients, meticulous preoperative preparation; optimal anesthesia, thorough, definitive, and expeditious operative technique, and rigid postoperative supervision. The selection of patients has been discussed. Other features will be reviewed separately.

Preoperative Preparation. After proper selection of the patient, it is mandatory to place that patient in the best possible condition in order to minimize surgical risk. Most patients coming to surgery are already *digitalized*. Excessive or inadequate medication must be corrected. Previous experience with the individual patient dictates the choice of preparation. Failure or fibrillation indicates the need for digitalis. A few patients with normal sinus rhythm may present no specific indication for digitalis. However, experience has shown that approximately half of them fibrillate after operation. Therefore, patients should be digitalized routinely.

In addition to rest and digitalization, the optimal state of compensation involves electrolyte balance, salt restriction, and the judicious use of *diuretics*.

Wilson and Moore have documented elevated total exchangeable sodium in cardiac patients even after prolonged salt restriction and diuresis. Hence, even in the presence of low serum-sodium levels, fluid restriction will usually restore a physiologic state. Intravenous saline is rarely indicated.

Diuretics will aid in attaining a "dry weight." Mercurial diuretics are contraindicated if there is any question of digitalis toxicity. These diuretics are rendered more effective by appropriate combination with ammonium chloride and aminophylline. As a test dose, 1 ml of Mercuhydrin is given intramuscularly. If there is substantial diuresis indicated by a weight loss of more than 2 lb, repeated doses are given. Mercurial diuretics may cause excessive fatigue, therefore, repetitive doses should be at least 2 days apart. They should not be given within 48 hr of operation. Elastic stockings aid fluid mobilization and decrease venous stasis in the legs.

Throughout the preoperative period, salt intake is restricted. A *400-mg sodium diet* seems optimal. Group IV patients, in addition to myocardial and pulmonary changes, often exhibit varying degrees of hepatic insufficiency. A diet high in carbohydrate, low in fat, with 40 to 50 Gm of protein is supplemented by parenteral vitamin B complex and folic acid.

In some situations, *anticoagulants* should be given prior to operation. It is preferable to maintain the anticoagulant effect as long as possible, restoring a normal clotting mechanism just prior to surgery with vitamin K_1 oxide.

Associated diseases, such as thyrotoxicosis and subacute bacterial endocarditis, should be controlled by available medical means. Once this is accomplished, operation may be undertaken.

Anesthesia. All surgical patients should arrive in the operating theater relaxed, comfortable, and confident. Much of this desired end can be accomplished by the surgical team. Cardiac surgery will probably never be "commonplace." The individual is understandably concerned by the knowl-

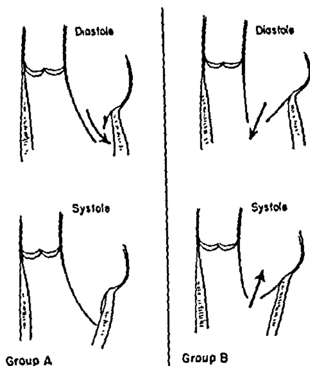


Fig. 7-56. Group A: Fishmouth opening of stenotic mitral valve funnel directed *laterally* so that it is closed by myocardium in systole, no regurgitation. Group B: Fishmouth opening of stenotic mitral valve funnel directed *medially* into outflow tract and *not* closed in systole; marked regurgitation.

between types I and II, and at the same time have any variation in the directional configuration between groups A and B. The tendency to scoop blood from the outflow tract will be increased if there is an unusually long minor leaflet and a smaller major leaflet, thus moving the opening into the aortic outflow tract

The concept of *secondary stenosis* is important Either type I or type II leaflet fusion may be associated with subleaflet fusion of chordae tendineae and papillary muscles. This additional zone may indeed pose more of a barrier to forward flow than does the primary stenosis In other words, mitral stenosis can be caused by fusion of the leaflets, the chordae, the papillary muscles, or all three This is why one must think in terms of valvuloplasty rather than in terms of simple opening of the commissures.

In this hemodynamic and surgical era it has become necessary accurately to differentiate severe mitral insufficiency from mild or moderate regurgitation, for mild or moderate grades of incompetence associated with dominant stenosis have shown improvement following surgery which is comparable to that of the "pure" stenosis. Indeed, some lesser degrees of leak are found to diminish with good valvuloplasty for stenosis. Simple expedients such as the use of an *extrinsic baffle*[1] will likewise reduce reflux.

Of equal significance to the complete understanding of mitral valvular problems has been consideration of related conditions which may obscure clinical evaluation. Noteworthy is the triad, "thyrotoxicosis, aortic insufficiency, and rheumatic activity." The patients may look thyrotoxic but are easily evaluated and generally found not to be. Left sternal border diastolic murmurs are often associated with pulmonic, not aortic, insufficiency. Finally, the factor of myocarditis, if present, is better tolerated without the added mechanical burden of stenosis.

Clearer scrutiny of patients reveals that most of those diagnosed as having "pneumonia" or "virus infection" actually have purulent pulmonary edema.

The surgical era has added new words and phrases with added hemodynamic significance to the cardiologists' vocabulary. "Valvuloplasty" and "commissurotomy" were among the first.

Additional descriptive phrases indicate better understanding of the hemodynamics involved in auscultatory phenomena, for example, "the mitral diastolic murmur of insufficiency" or the "high-pitch, low-flow systolic murmur of mitral stenosis." These seem paradoxical, but review of the kinetic pathologic or hemodynamic circumstances affords clarification. When the mitral valve is freely incompetent, the left atrium undergoes marked dilatation. The ventricle must also dilate to compensate for the reflux Thus, if a heart is to put out 4 liters of blood and there is a reflux of 8 liters a minute, a total of 12 liters must pass from atrium to ventricle every minute during diastole. This large flow rushing through an annulus, albeit

[1] The extrinsic baffle consists of a hard roll of Gel-Foam of a firm consistency that resists absorption It is 2 to 4 cm in diameter and 5 to 9 cm in length. It is placed on the posterior and lateral aspects of the left atrium above the AV groove to reduce the herniated valve complex. This in effect increases the effective leaflet length and corrects the relative shortening of chordae tendineae, allowing better valve closure. In some instances, distortion of the annulus is possible to improve leaflet closure. Further discussion of this pathologic pattern is included in the section describing atrial contours at fluoroscopy.

At this point the atrium is inspected The position, size, and shape are observed. Thrombosis or calcification is noted. The coronary *arteries are* visualized The size of the right and left ventricles and pulmonary artery is observed. Two opposing *purse-string* sutures of oiled No. 0 black silk on *an atraumatic* swedged needle *are then placed* about the base of the auricle These sutures *should* be so placed that when tied they smoothly amputate the auricle at its base on the left atrium. If there is no clot in the atrium, the base of the auricle is grasped *with the appropriate* atrial clamp, the tip of the auricle is amputated, and trabeculae carnae are divided The incision in the tip of the auricle is enlarged so that it will comfortably admit the surgeon's index finger. Each side of the auricle is *then grasped* with a right-angle clamp for stabilization. If clot is present within the auricle, the tip is amputated without securing hemostasis with an atrial clamp The atrium is allowed to flush freely to remove loose clot The removal of clot may be implemented by use of an *open-tip* suction tube. *The base* is then secured with the proper atrial clamp, the incision enlarged, and subsequent flushing carried out as indicated. Having prepared the atrium, the assistants stabilize the auricle by means of the previously placed *right-angle clamps and provide* countertraction as the surgeon's finger is inserted *into* the auricle Hemostasis is maintained by traction on a purse-string suture. The intracardiac finger determines the type, position, and size of the mitral orifice as well as the *presence* of any *associated* anomaly such as septal defect, intracardiac tumor, etc.

Finger fracture of the fused anterior commissure is initiated by anterolateral pressure with the tip of the finger (Fig 7-59) The initial fracture *is* extended to the annulus *anteriorly by gentle blunt dissection. Helpful* external counterpressure may be *provided* on the anterolateral aspect of the ventricle by the surgeon's left hand or by an assistant delivering pressure through a folded sponge. If a satisfactory opening is obtained by this *maneuver* (valve area of 4 cm² or *more*), *the* posterior commissure need *not be opened However*, if the surgeon feels that regurgitation will not be produced by opening the posterior fusion bridge and that further increase in the valve size is *indicated*, it can be accomplished by posterolateral *pressure*, rotating toward the aortic *leaflet This fusion* bridge is important but *treacherous If* it is small, and a good valve orifice has been attained, this bridge is left unopened, particularly if it is *heavily* calcified or if there is significant regurgitation in this area Conversely, if it is long and *contributes* greatly to the stenosis, it should be *carefully* but

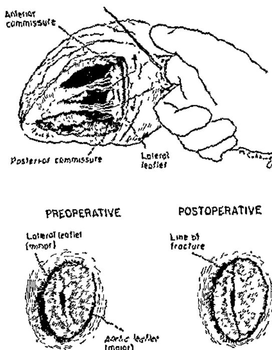


Fig. 7-59. Technique of "finger-fracture valvuloplasty." Fracture is initiated by anterolateral pressure away from the aortic leaflet, then, if necessary to open posterior commissure, posterolateral pressure rotating toward the aortic leaflet; leaflets are then completely mobilized by blunt dissection through fused areas to the annulus More crescentic fracture lines give greater major (aortic) leaflet opening and flutter valve action. The posteromedial fracture is generally obtained by pressure on the opposite side

completely opened The surgeon may need to *change to the* opposite side of the table and use the bare finger to accomplish this part of the valvuloplasty

If the valve *resists* "finger fracture," separation *may be* initiated with the Harken No. 9 valvulotome This is more often required in type II valves The anterior edge of the auricular *stump* is grasped with a right-angle clamp The blade of the valvulotome *is advanced* along the palmar *surface of the index* finger into the auricle As the *twist of the handle* reaches the purse-string *sutures, the* valvulotome is rotated so that the serrated cutting edge is anterior and the handle lies flat against the *surgeon's thenar* eminence. During this *maneuver*, the purse-string sutures are *controlled by the first* assistant The valvulotome is *stabilized by* grasping its handle against the *base of the index* finger with the thumb and *may be further stabilized* by the surgeon's left hand. Incision is accomplished by *moving the finger* and

present no evidence of frank right ventricular failure.

Group III includes patients whose disability is *progressive* rather than static. There may be increasing dyspnea on effort or easily provoked attacks of hemoptysis, chest pain, and pulmonary edema. They may suffer from palpitation, tachycardia, and distress over the liver upon exertion. At any time they may slip into group IV or may die in an acute attack

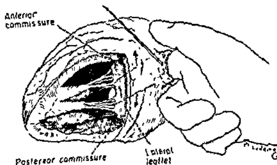


Fig. 7-57. Chest films in a case of mitral stenosis.

At this point the atrium is inspected The position, size, and shape are observed. Thrombosis or calcification is noted. The coronary arteries are visualized The size of the right and left ventricles and pulmonary artery is observed Two opposing purse-string sutures of oiled No 0 black silk on an atraumatic swedged needle are then placed about the base of the auricle These sutures should be so placed that when tied they smoothly amputate the auricle at its base on the left atrium. If there is no clot in the atrium, the base of the auricle is grasped with the appropriate atrial clamp, the tip of the auricle is amputated, and trabeculae carnae are divided The incision in the tip of the auricle is enlarged so that it will comfortably admit the surgeon's index finger. Each side of the auricle is then grasped with a right-angle clamp for stabilization If clot is present within the auricle, the tip is amputated without securing hemostasis with an atrial clamp The atrium is allowed to flush freely to remove loose clot. The removal of clot may be implemented by use of an open-tip suction tube The base is then secured with the proper atrial clamp, the incision enlarged, and subsequent flushing carried out as indicated Having prepared the atrium, the assistants stabilize the auricle by means of the previously placed right-angle clamps and provide countertraction as the surgeon's finger is inserted into the auricle. Hemostasis is maintained by traction on a purse-string suture. The intracardiac finger determines the type, position, and size of the mitral orifice as well as the presence of any associated anomaly such as septal defect, intracardiac tumor, etc

Finger fracture of the fused anterior commissure is initiated by anterolateral pressure with the tip of the finger (Fig 7-59) The initial fracture is extended to the annulus anteriorly by gentle blunt dissection Helpful external counterpressure may be provided on the anterolateral aspect of the ventricle by the surgeon's left hand or by an assistant delivering pressure through a folded sponge. If a satisfactory opening is obtained by this maneuver (valve area of 4 cm^2 or more), the posterior commissure need not be opened However, if the surgeon feels that regurgitation will not be pro-

rotating toward the aortic leaflet This fusion bridge is important but treacherous If it is small, and a good valve orifice has been attained, this bridge is left unopened, particularly if it is heavily calcified or if there is significant regurgitation in this area Conversely, if it is long and contributes greatly to the stenosis, it should be carefully but



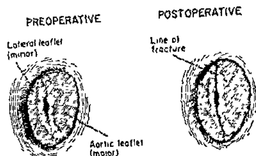


Fig. 7-59. Technique of "finger-fracture valvuloplasty." Fracture is initiated by anterolateral pressure away from the aortic leaflet, then, if necessary to open posterior commissure, posterolateral pressure rotating toward the aortic leaflet; leaflets are then completely mobilized by blunt dissection through fused areas to the annulus. More crescentic fracture lines give greater major (aortic) leaflet opening and flutter valve action. The posteromedial fracture is generally obtained by pressure on the opposite side.

completely opened. The surgeon may need to change to the opposite side of the table and use the bare finger to accomplish this part of the valvuloplasty

If the valve resists "finger fracture," separation may be initiated with the Harken No. 9 valvulotome This is more often required in type II valves The anterior edge of the auricular stump is grasped with a right-angle clamp. The blade of the valvulotome is advanced along the palmar surface of the index finger into the auricle. As the twist of the handle reaches the purse-string sutures, the valvulotome is rotated so that the serrated cutting edge is anterior and the handle lies flat against the surgeon's thenar eminence. During this maneuver, the purse-string sutures are controlled by the first assistant. The valvulotome is stabilized by grasping its handle against the base of the index finger with the thumb and may be further stabilized by the surgeon's left hand. Incision is accomplished by moving the finger and

tion in the offending right ventricular dilatation and hypertrophy.

Active rheumatic carditis remains as a firm contraindication to the surgical correction of mitral stenosis. On the other hand, when "rheumatic activity" is only suspected, one should not hesitate to proceed with operation. It is reasonable to assume that elimination of the stenosis will reduce strain on the myocardium and cause rheumatic activity to be better tolerated. Low-grade fever and joint pains usually are less frequent following surgery. In the event that rheumatic carditis does develop during the postoperative period, salicylates and corticosteroids may be used.

Associated diseases, such as *arteriosclerotic* and *hypertensive cardiovascular disease* undoubtedly increase surgical risk. This is particularly true of coronary artery disease. However, individuals with other diseases may tolerate them better without the burden of mitral stenosis

Within the framework of the above classification and conditioning factors, we believe that the physician who recognizes symptomatic mitral stenosis should consider it his obligation to seek proper evaluation of the patient with a view toward surgical correction Furthermore, he is obliged to expedite his patient's treatment before the patient slips from the low-risk category (group III, 0 6 per cent) to the high-risk group (group IV, 20 per cent). Multivalvular problems must have careful evaluation to determine hemodynamic dominance of the components.

SELECTION OF PATIENTS FOR OPERATION

Criteria for the selection of patients for operation have broadened but not changed in principle. Patients should not have surgery unless they are disabled by their disease. If they are becoming progressively worse in spite of medical treatment, the indications for surgical help are more urgent. When there is a benign form of mitral valve disease, it is usually difficult to foretell what the course of the illness will be before the onset of symptoms. It must be remembered also that mitral operation, in its present form, is a palliative pro-

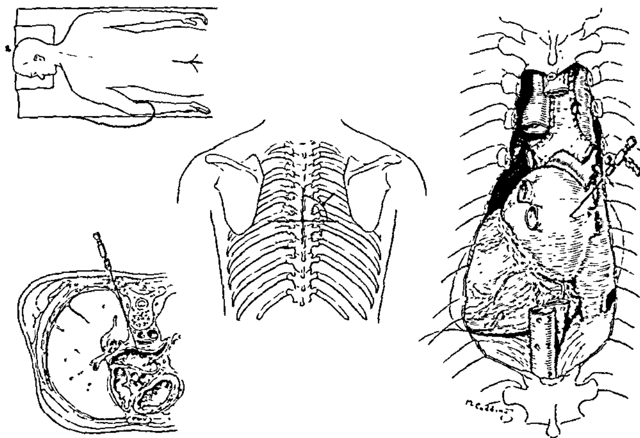


Fig. 7-58. Technique of left heart catheterization performed under local anesthesia through the right posterior thorax with the patient prone on a fluoroscopic table.

This is generally on the third to the fifth postoperative day.

Early ambulation is advocated, and patients *are usually* up the day after surgery.

Patients are routinely discharged on a strict cardiac regimen This includes a low sodium diet, maintenance digitalis, an adequate diuretic program, quinidine prophylaxis as indicated, prophylactic antibiotics. Such a regimen is tapered as tolerated by the patient. Patients in atrial fibrillation, of course, remain on digitalis. Initial improvement is dramatic, but a plateau is seldom reached before a year following surgery. These patients are advised to increase their activity to the point of slight fatigue but never to exhaustion *It should be* emphasized that, during the postoperative period when the left ventricle is being "trained" to accept a normal work load, strict adherence to a full medical regimen is absolutely *necessary It is difficult* to impress this fact upon the patient, and occasionally the inexperienced physician fails to appreciate its importance. However, the propriety of such a program is indubitable

RESULTS IN THE FIRST 1,000 CONSECUTIVE VALVULOPLASTIES

The results of "total surgical management" have been reported by Ellis (1957) in a survey of patients studied for 1 to 7 years Of this first 1,000 patients, 913 survived operation, an over-all mortality of 8 7 per cent

Among group III patients the mortality in the first 100 was 14 per cent This has steadily declined to a gratifying 0 6 per cent in the second 500 patients Conversely, group IV patients have not shown the same dramatic mortality reduction, i.e., 32 per cent in the first 100 to 20 per cent in the second 500 (Table 7-10) Subsequent *experience* in the past year does not appear to alter these mortality figures significantly

Ellis' study shows that 78 per cent of the patients in group III and 62 per cent of group IV patients showed significant postoperative improvement The degree of improvement in group III patients has been maintained over a follow-up time *of 8 years* Thus the improvement from operation is persistent, and the number of significant regressions is small *The* same is true for group IV patients The *difference* in the degree of improvement in group III *patients after* 8 or more years is not significant However, it is our clinical impression that more complete valvuloplasty has been *performed* as *experience* has increased. This should result in fewer recurrences and more complete rehabilitation. In all probability the technical advances in quality of valvuloplasty have kept pace with the improvement in mortality.

TABLE 7-10. OPERATIVE MORTALITY

Patients	*Mortality, per cent*	
	Groups II, III	*Group IV*
1–100	14.0	34
101–500	4.0	24
501–1,000	0 6	21

It is always important to compare the life cycle of surgical patients *with those similarly* afflicted who were treated medically. The only series comparable *to the authors', of which* they are aware, is that of Oleson. The medical treatment enjoyed by these individuals was remarkably thorough and similar to that currently available. Of these patients, 176 were classified according to the American Heart Association *in class 3 or were fibrillating* patients in class 2, and 52 were in class 4. These are comparable to our groups III and IV. The average age and sex distribution are almost exactly the same as in the authors' patients. What then are the results in the series of operated patients as compared to Oleson's medically treated patients over a 7-year period? Of the medically treated patients, 51 per cent survived for 7 years, in the surgically treated patients, survival rate was 87 per cent after 7 years, including an operative mortality of 3 per cent. Thus the survival rate in the operated patients was significantly better than in Oleson's group.

The group IV patients have been similarly *compared* and gave even more striking *results In the* group of operated patients, survival rate has been 54 per cent at the *end of* 7 years, including the high early operative mortality of 24 per cent Only 6 per cent of Oleson's medically treated patients were alive at the end of 7 years. In comparing the two groups, the operated *patients are still* better off as far as *survival is* concerned even at the *end of the* first year of observation, which in-

edge that "the citadel of his very existence" is being approached. Much of this fear can be dispelled by deleting phantasy and establishing a firm rapport between the surgeon, his associates, and the patient.

Choice of premedication is of prime import. The patient must be sedated but not depressed. *Barbiturates* in amounts of 50 to 100 mg supplemented with a similar amount of *Demerol* are usually adequate. Atropine and scopolamine are contraindicated because vagal depression may result in tachycardia, which is deleterious to an individual with mitral stenosis. Tachycardia shortens diastole, increases right heart output, and in the presence of associated mitral insufficiency, increases the total volume regurgitated into the atrium. The result is decreased cardiac output and increased pulmonary hypertension, even pulmonary edema. This is a common complication of anesthesia and surgery

Prior to inducing anesthesia, the patient is connected to a cardioscope or direct-writing electrocardiograph so that continual monitoring by anesthesiologist and cardiologist is possible. Electroencephalograms are interesting and useful but not essential.

The belief in and implementation of the dictum "maximum oxygenation and minimal agent" is of greater importance than the choice of agent These patients need only to be narcotized, not anesthetized. At the conclusion of the operation, they must be awake and responding to command. In general, Pentothal 100 to 200 mg followed by ether, nitrous oxide, and oxygen are used One ounce of ether is usually more than enough for an operation.

Operation. In the authors' opinion, the best approach for pure mitral stenosis is through a standard left parascapular incision, starting 2 cm to the left of the midline in the inframammary fold, passing 5 cm below the tip of the scapula, and extending vertically midway between the medial border of the scapula and thoracic spines to the level of the spine of the scapula.

The incision is deepened through the musculature to the rib cage Hemostasis is accomplished by clamp and cautery. The pleural cavity is entered through the 5th interspace, the fifth rib is divided posteriorly at the transverse process, and a 1-cm section is resected by means of a rongeur so that painful bony crepitus will be avoided once the chest has been reconstituted. The costal cartilage of the same rib is divided anteriorly, and the contributing branches of the intercostal vessel to the internal mammary artery are clamped and ligated Posteriorly, the 5th intercostal bundle is isolated, clamped, divided, and secured by ligatures. The edges of the operative incision are freshly draped, and the ribs and incision are spread by means of a Harken retractor.

If the innomiate and left carotid arteries are to be isolated in order to prevent cerebral embolism, the dissection is carried out at this point. Originally, the authors thought that all patients who might sustain embolization should have head vessel isolation. This meant all patients over 40, all who were fibrillating, all who had had emboli in the past, and all who showed clot or calcification in the atrium or valve. However, the isolation of these structures is not wholly benign. Furthermore, the proper time to occlude cerebral circulation to prevent embolus from atrial clots is impossible to determine. Since clots may be dislodged and migrate at any time during the operation, the initial program seems unnecessary and undesirable. The authors now reserve head vessel isolation for those instances when there is calcification in the valve. In such a situation, the head vessels are occluded for periods of 20 sec following any manipulation which might dislodge calcific particles which could embolize centrally.

The cerebral vessel isolation is carried out as follows: The mediastinal pleura is incised just above the arch of the aorta. The innominate artery and the left common carotid artery are cleared by blunt dissection. Penrose tubes are then placed about each vessel. Subsequently, during the operation when interruption of the cerebral circulation is desired, traction on the Penrose tubes angulates and occludes the vessels. It is well to ask the anesthesiologist to confirm interruption of the circulation by palpation of the carotids in the neck while the surgeon interrupts blood flow by angulating the vessel. It is equally important that the anesthesiologist report restoration of the carotid pulse once traction has been released. Care must be exercised to avoid inadvertent traction.

The pericardium is opened parallel and 2 cm posterior to the phrenic nerve from a point some 4 cm below the AV groove and upward some 12 cm to a point well over the pulmonary artery. Four pairs of No. 0 black silk sutures are placed opposing each other in the cut edges of the pericardium These "marsupializing" sutures serve to rotate and stabilize the heart and hold the pericardium open. The anesthesiologist reexpands the lung at this time; then it is gently retracted behind a moistened saline sponge as the heart is stabilized by placing tension on the marsupializing sutures Anteriorly, these sutures are attached to the chest wall, [illegible] they are stabilized over the rib spr[illegible]
from the heart [illegible]
clean towels, and preparations for the intracardiac phase are then complete.

15

Surgery of mitral insufficiency

HENRY THOMAS NICHOLS AND CHARLES P. BAILEY

INTRODUCTION

Mitral insufficiency probably is second only to mitral stenosis as the most common lesion of the heart valves Apparently the initial valvular lesion in rheumatic fever usually is a regurgitant one. As the pathologic condition of the valve "heals," however, *stenosis* becomes more common, seeming to overcome or replace the regurgitation In the 730 cases followed by Bland, 18 per cent had mitral stenosis, 16 per cent had mitral insufficiency, and 55 per cent had a combination of both elements of valvular dysfunction There seems to be some doubt as to the role played by mitral insufficiency, per se, in the patient who succumbs during an acute rheumatic episode Some feel that these deaths are due primarily to acute myocarditis and that the valvular lesion plays little or no part Others feel that the mitral insufficiency plays a major role in producing the cardiac failure and ultimate death *Eventually this* question may be answered if attempts should be made to correct the regurgitation surgically during the course of acute rheumatic activity We know of no such intervention

There is no doubt that mitral insufficiency can and does produce death in the absence of acute myocarditis This *is seen in cases of* "pure" mitral insufficiency in which the rheumatic process has long been quiescent It is demonstrated typically in patients in whom mitral regurgitation of a major degree is created *during the* surgical relief of "pure" mitral stenosis. The seriousness of an associated element of insufficiency is well known to the cardiac surgeon who adequately relieves the obstruction in a case of combined mitral stenosis and regurgitation. If the mitral insufficiency is more than of minor degree, the patient will not receive significant clinical benefit.

ETIOLOGY AND PATHOLOGY

Congenital perforation of one or both mitral leaflets can occur and produces mitral insufficiency. *However, this is a rare condition.* The authors have recognized it in only three instances.

It is more common to encounter *mitral insufficiency* due to a *congenital cleft leaflet*, but all the authors' cases have been associated with low atrial septal defects due to incomplete fusion of the endocardial cushions.

Detachment of the chordae tendineae gives rise to mitral insufficiency, but this lesion is rare, except when produced traumatically during the surgical relief of mitral stenosis. *Rupture or detachment of a papillary muscle* as *a result of coronary artery occlusion with subsequent* muscle necrosis also can lead to mitral regurgitation. Fortunately, this too is rare

Bacterial endocarditis may cause an erosion defect of the leaflets and produce mitral insufficiency The aftermath of such an infection can be marked scarring of the leaflets or the *chordopapillary supports.* Bacterial endocarditis rarely involves a valve that has not been deformed congenitally or damaged *previously* by rheumatic fever.

Certainly the over-all most common cause of incompetence of the mitral valve is *the rheumatic process* As stated previously, during the acute phase of rheumatic fever, mitral

valvulotome as one unit. This instrument is not used as a saw. Its most effective cutting direction is downward and forward against the anterior fusion bridge. This motion anteriorly and caudally protects the valve leaflets and chordae. Care is exercised to avoid extending the incision through the annulus and the AV groove. Once separation has been started, it can be extended by finger fracture. These maneuvers should adequately separate the fused commissures.

The valve complex is then examined for secondary stenosis, which is present in over 30 per cent of patients. Fusion of chordae tendineae and papillary muscles, when present, is separated by longitudinal or rotational blunt dissection with the operating finger. Great care is exercised to avoid division of salient leaflet moorings lest regurgitation be created. Guillotine valvulotomes are prone to produce regurgitation since tactile control is compromised and salient leaflet moorings or chordae are often caught in the instrument. The use of this type of instrument is rarely needed. Once the fused chordae are separated, the dissection is carried distally to mobilize any fused papillary muscles *Valvuloplasty is complete only when the mitral orifice has been optimally enlarged throughout and maximum mobility of the mitral leaflets has been restored without the production of regurgitation.* An "excellent valvuloplasty" unfortunately is a relative term, depending too much upon the experience, skill, and patience of the surgeon.

As the surgeon's finger is withdrawn, the opposing purse-string sutures are tied by assistants and the base of the auricle is further secured by a tertiary ligature of No 0 black braided silk The redundant portion of the auricular stump is trimmed away and the margins oversewn by a continuous suture of No. 0 atraumatic silk.

The lung is reexpanded and the pericardium closed loosely by tying the opposing marsupializing sutures A No 28 red rubber tube is placed through the 9th interspace in the midaxillary line and attached to underwater seal drainage The rib cage is approximated by six pairs of doubled No. 0 chromic catgut pericostal sutures. The divided costal cartilage is reconstituted with the same material. Muscle and fascial layers are closed with continuous sutures of No. 0 chromic catgut, the subcutaneous tissue with continuous No 00 chromic catgut, and the skin with a continuous No. 000 black silk suture If the anesthesia has been properly administered, the patient should be semiconscious and responding to commands as the final skin sutures are placed. This procedure should routinely take about 1 hr. Expeditious surgery is always important. Hurried surgery, just as wasted operating time, must be avoided.

The patient is moved to his own bed directly from the operating table and placed in semi-Fowler's position. Continuous oxygenation is maintained by the anesthesiologist. This is accomplished by the intratracheal tube until extubation and then by nasal catheter. Fowler's position reduces the weight of the abdominal viscera on the diaphragm and favors ventilation. Nasal oxygen is continued for a minimum of 24 hr and thereafter as indicated. Maximum oxygenation is assured by strict attention to tracheal toilet. Ideally this is accomplished by the patient's own efforts either by spontaneous or induced coughing Tracheal suction is routinely accomplished twice daily for 2 days, then as indicated. Early in the postoperative period, the patient resumes his *specific remedial breathing exercises.* These are continued for at least 1 month after discharge from the hospital.

Occasionally, in addition to blood replacement, supportive therapy to correct hypotension is indicated. In acute changes, *Neosynephrine* and *ephedrine* are useful. *Norepinephrine,* as a slow intravenous drip, is better for prolonged use.

Parenteral *penicillin,* 600,000 units twice daily, is administered for the first six postoperative days, and thereafter the patient is placed on permanent prophylactic oral penicillin 200,000 units daily. This permanent penicillin program is intended to reduce the incidence of recurrent rheumatic fever.

The maintenance dose of *digitalis* is continued following operation. Supplementary digitalis is often necessary during the first 24 to 36 hr in order to control tachycardia. This is accomplished by repeated small doses of rapidly acting glycosides such as *Lanoxin* (digoxin), *Cedilanid,* or *ouabain.* Patients in normal sinus rhythm prior to and during surgery are given prophylactic *quinidine* in doses of 0.3 Gm at 6-hr intervals. In spite of this prophylaxis, almost half the patients develop atrial fibrillation during the first postoperative week. At this time, quinidine is omitted and supplemental digitalis is used to control any existing tachycardia. Seven to ten days later an attempt is made to revert these patients to normal sinus rhythm by administering increasing doses of quinidine under appropriate electrocardiographic control. This is generally successful. Alteration in sodium, potassium, and nitrogen balance normally occurring following surgery is accentuated following cardiac operations. It is important to restrict fluid (1,000 to 1,500 cc of 5 per cent glucose in water a day) until the postoperative diuresis occurs

tion of the left ventricular stroke volume *regurgitates* through the mitral valve *into the* left atrium, adding to the normal content of this chamber. During the following ventricular filling period, the left ventricle is faced with *an increased volume load: the right* ventricular stroke volume plus *the left regurgitant* volume. The *increased* volume load causes a lengthening of the left ventricular fibers and, according to Starling's law, *produces* a more forceful ventricular contraction, thus helping to maintain a normal or but moderately *reduced forward cardiac* output. *As a consequence of the increased work, the left ventricle dilates, hypertrophies, and eventually may fail.*

These concepts have been challenged recently on *the basis of clinical and* experimental data by a *number of investigators* who fail to find left ventricular dilatation in *certain* cases (Braunwald et al; Grant et al.) Whether there *actually is no* ventricular dilatation, or *whether it is our inability accurately* to measure it, is open to question. Certainly dye studies, *isotope* administrations, and ventriculography fall short of quantitative accuracy. However, many patients with marked *mitral* insufficiency are seen in whom the left ventricle seems to be slightly if at all enlarged or dilated when viewed at *surgery*

There are several factors *which may* be *responsible for* this lack of obvious *ventricular* dilatation. (1) There is a decreased effective cardiac output (into the aorta) as measured by cardiac catheterization Thus, *the ventricle is not so dilated as to* accommodate both the regurgitant flow and a *normal stroke output.* (2) The diastolic lengthening *of the* ventricular muscle *fibers,* however small, *initiates a* more complete *or prolonged* systolic effort so that *there* is an *encroachment upon* the endsystolic volume of the left ventricle (3) The early diastolic ventricular volume is *even* less than the already lowered end-systolic ventricular *volume because,* even *after the* aortic valve has closed, *blood continues to be ejected into* the left atrium until the left ventricular *pressure falls* to the level *of that* of the left *atrium The modalities* by which the left ventricle compensates *or fails to compensate* require further investigation.

There *seems* to be general *agreement* that *mitral insufficiency of clinical significance is accompanied* by a low *cardiac output.* This output may be adequate at rest but, *during* exercise, does not increase sufficiently to keep pace with the *bodily demands.* A state of relative hypoxia develops and it, plus an *environment* of acid metabolites, *probably accounts* for the *fatigue* which is the most *common* symptom of mitral regurgitation.

In mitral insufficiency, the left atrium undergoes phasic increases of volume and pressure which are synchronous with left ventricular systole, and the magnitude of these increases *depends upon the interplay of several* factors: the volume and *velocity of the regurgitant* jet, the volume of the left atrium, the elasticity of the left atrial wall, and the magnitude of the pulmonary venous return Other factors being *equal, a more rigid left atrium resists dilatation,* producing higher *phasic* intra-atrial pressure. This higher pressure *is transmitted* backward into the pulmonary *capillaries. Whether this elevation* of the pulmonary capillary and pulmonary *venous pressure is* related directly to the symptom *of dyspnea* is not known. Clinically, the patient *with a small* relatively nondistensile left atrium *appears to* complain of dyspnea *much* more often than *the patient with an enlarged, elastic left* atrium.

The impact of the phasic or, *when left* ventricular failure occurs, sustained *left atrial hypertension, transmitted* backward through the pulmonary *veins, is responsible* for the *initiation of pulmonary vascular* changes which *are* identical with *those of mitral* stenosis (Becker et al) The resistance to the flow of blood through the narrowed pulmonary *vessels* increases, and *pulmonary* arterial and *right ventricular hypertension* ensues. The right ventricle *hypertrophies* and *finally fails.*

SYMPTOMATOLOGY

Symptoms. The most *common symptom* of *mitral insufficiency is fatigue.* It was the foremost symptom in previous reports *concerning* 124 cases, and in a more recent analysis of 70 cases (Uricchio et al.). Fatigue *is usually* the *first symptom to appear* and *is the most disturbing to the patient. In our series, it was* present in 90 per cent and *was deemed to be* related to a low cardiac output. *It* should be pointed out that the majority *of our* patients fall *within the third, fourth,* and fifth *decades* of life.

Exertional dyspnea, as reported *previously, is of* but moderate *severity* and appears late in *the course* of the disease. During exertion, the

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In mitral insufficiency, the left atrium undergoes phasic increases of volume and pressure which are *synchronous with left ventricular systole*, and the magnitude of these increases depends upon the interplay of several factors: the volume and *velocity of the regurgitant* jet, the volume of the left atrium, the elasticity of the left atrial wall, and the magnitude of the pulmonary venous return Other factors being equal, a more rigid left atrium resists dilatation, producing higher phasic intra-atrial pressure. *Thus higher pressure is transmitted* backward into *the pulmonary capillaries. Whether this elevation of the pulmonary capil*lary and *pulmonary* venous pressure is related directly to the symptom of dyspnea is not known. Clinically, the patient with *a small* relatively *nondistensile left atrium* appears to complain of dyspnea much more often than the patient with an enlarged, elastic left atrium.

The impact of the phasic or, when left ventricular *failure occurs, sustained* left atrial hypertension, transmitted *backward through* the *pulmonary veins, is responsible for* the initiation of pulmonary vascular changes which are identical with those of *mitral* stenosis (Becker et al.). The resistance to the *flow* of blood through the narrowed pulmonary vessels increases, and pulmonary *arterial* and *right ventricular hypertension* ensues. The *right ventricle hypertrophies* and finally fails.

SYMPTOMATOLOGY

Symptoms. The most common symptom of mitral insufficiency is *fatigue* It was the foremost symptom in *previous reports* concerning 124 cases, and in a more recent analysis of 70 *cases (Uricchio* et al.). Fatigue *is usually the* first *symptom to appear and is the most dis*turbing to the *patient. In our series,* it was *present in* 90 per cent and was deemed *to be* related to a low cardiac output. *It should be* pointed out that the *majority* of our patients fall within the third, fourth, and fifth *decades of life.*

Exertional dyspnea, as reported previously, is of but *moderate severity* and appears late in the course of the disease. *During exertion,* the

cluded all the operative mortality. The difference between the survival of operated and medically treated patients is so striking in both groups III and IV that it is evident that valvuloplasty has increased life expectancy. Moreover, and even more important, the *operated patients have lived lives of much greater comfort and usefulness in contrast to the characteristic deterioration under medical management,* as reflected in Oleson's curves. This is predicated on the fact that the majority of deaths of patients under medical care are not sudden deaths.

Extensive calcification was feared initially, and that fear has been justified. It was thought that such valves would be more likely to cast off *emboli* at the time of fracture, would be less well mobilized, and that the rate of recurrence might be higher Embolization has *been reduced by appropriate diversion of* blood flow away from the brain immediately after fracture and by more skillful fracture. However, the long-term *improvement is less,* by just over 10 per cent, in both the group III and IV patients.

One of the most striking benefits of valvuloplasty has been the dramatic reduction in emboli. Of the first 1,000 patients, 190 had had one or more definite embolic episodes prior to operation, whereas in a total of approximately 3,000 patient follow-up years after surgery, there have been but 21 probable embolic episodes This indicates that embolization is an indication for surgery, and repeated embolization may constitute an indication for *emergency valvuloplasty In all instances of* emergency valvuloplasty (three or more emboli within 4 days), embolization has stopped with the removal of the auricle, flushing of the atrium, and correction of stasis in the atrium by relieving the stenosis. Fortunately, there have been no operative deaths in this group. This points up the error now being made in some areas of considering recent embolism a contraindication to surgery.

Twenty-seven women were *operated during pregnancy.* This experience indicated that there is a place for surgical correction of the mitral stenosis in women unable to negotiate pregnancy safely on a medical program. There were three deaths: two unrelated to the pregnancy (cerebral embolism and ventricular fibrillation) and the third due to an error in diagnosis. This third patient had active rheumatic carditis and succumbed subsequently following surgical abortion. This error in diagnosis was due to failure to appreciate that *the diagnosis of stenosis* during pregnancy is unreliable. While a valid case can be made for the interruption of pregnancy and subsequent valvuloplasty, this is an unattractive approach to us. If the patient has had a diagnosis of mitral stenosis made before pregnancy by competent individuals, and that patient is in group III, we would favor one definitive operation that corrects the stenosis and salvages the pregnancy.

After reviewing the remarkably satisfactory results of valvuloplasty in the group III category and the formidable increase *in risk when* the patient *is "followed" to the group* IV phase, one can only conclude that such procrastination constitutes a dereliction of duty. Con*versely, prophylactic* valvuloplasty cannot be condoned. This is not definitive surgery as in the closure of a persistent ductus arteriosus.

tion of the left ventricular stroke volume regurgitates through the mitral valve into the left atrium, adding to the normal content of this chamber. During the following ventricular filling period, the left ventricle is faced with an increased volume load: the right ventricular stroke volume plus the left regurgitant volume. The increased volume load causes a lengthening of the left ventricular fibers and, according to Starling's law, produces a more forceful ventricular contraction, thus helping to maintain a normal or but moderately reduced forward cardiac output. *As a consequence of the increased work, the left ventricle dilates, hypertrophies, and eventually may fail.*

These concepts have been challenged recently on the basis of clinical and experimental data by a number of investigators who fail to find left ventricular dilatation in certain cases (Braunwald et al., Grant et al.). Whether there actually is no ventricular dilatation, or whether it is our inability accurately to measure it, is open to question Certainly dye studies, isotope administrations, and ventriculography fall short of quantitative accuracy However, many patients with marked mitral insufficiency are seen in whom the left ventricle seems to be slightly if at all enlarged or dilated when viewed at surgery

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In that form of mitral insufficiency which commonly is described as "functional," "relative," or "adynamic," the basic lesion may be the left ventricular dilatation associated with aortic stenosis, aortic insufficiency, or hypertension. Probably the pathologic changes often may be similar to those just described as occurring in the course of acute rheumatic fever. However, the mitral leaflets may be essentially normal.

The mitral regurgitation which has been created during the operative relief of mitral stenosis may be due to cutting or detaching the chordal supports to a leaflet, cutting into or perforating a leaflet instead of the fused commissures, extending of an accurate commissural incision beyond the chordal supports into a flexible area of leaflet tissue, extending the valvular incision to the point of complete division of the annulus fibrosus, or detachment of a leaflet from its attachment to the annulus.

In late rheumatic mitral insufficiency, the pathologic alterations of the mitral leaflets and their supporting structures can be quite varied and may be multiple in any given case It should be borne in mind that, in practically every instance, there is either an actual or a relative lack of leaflet substance which renders it impossible for the cusps to make marginal contact during ventricular systole. The three basic pathologic alterations are (1) dilatation of the mitral annulus fibrosus, (2) scarring and retraction of one or both leaflets, and (3) scarring and shortening of the chordopapillary supports.

Dilatation of the mitral annulus leads to separation of the leaflets. Since they arise from and are firmly attached to the annulus, the free margins may be unable to coapt during systole, permitting regurgitation to occur. An element of annular dilatation frequently complicates a case of mitral insufficiency which is due primarily to some other cause. As the heart enlarges in an attempt to compensate for left ventricular failure, the annulus becomes dilated, causing further increase in the incompetence. This phenomenon takes on all the characteristics of a vicious cycle.

Scarring and retraction more commonly involve the posterior or mural leaflet. However, the anterior or septal leaflet is by no means immune. The mural leaflet, in many rheumatic cases, shows a complete loss of mobility and acts merely as a rigid fibrotic or calcific ledge against which the mobile septal leaflet either makes or attempts to make contact. This immobility of the mural leaflet may be related in part to scarring and shortening of the chordae of the third order, which may even become adherent laterally to the adjacent left ventricular wall.

The primary and secondary chordae of both leaflets also may be shortened. Such involvement may result in a fixed depression of the leaflet edges within the left ventricular cavity, thus preventing contact during ventricular systole.

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X-ray. The cardiac size, as seen in the PA view is quite variable, but the vast majority of patients seeking surgical relief have shown a 3+ or greater enlargement. Usually *the left cardiac border is elongated.* Frequently, the aortic knob is less prominent than normal, because of clockwise rotation of the heart. *The pulmonary artery and left atrial arch are prominent on the left border. A double atrial contour is frequent on the right border of the heart.* The barium-filled esophagus frequently is deviated to the right, rarely to the left. Mitral valve *calcification may be* observed.

In the RAO and left lateral views, the *left atrium is enlarged* and, in the vast majority of cases, assumes a wide-sweeping curve which displaces *the barium-filled esophagus posteriorly.* In general, the left atrial enlargement in mitral insufficiency is much greater and extends farther downward than in mitral stenosis In some cases, the *left atrium actually becomes aneurysmal* and so enlarged as to dwarf the rest of the heart

The left ventricular size is difficult to assess even with lateral and oblique views. It must be borne in mind that the pericardium does not always remain in close proximity to the heart wall in mitral insufficiency Frequently, when the left atrium is greatly enlarged, the pericardium runs in a relatively straight line from the wall of the atrium to the apex of the heart instead of deviating inward *in the region of* the atrioventrioventricular groove. The space along the AV groove and the posterior surface of the left ventricle may be filled with pericardial fluid, which can be erroneously interpreted as enlargement of the left ventricle

Cardiac Catheterization. It was hoped that *right heart catheterization* would make it possible to diagnose mitral insufficiency correctly Theoretically, the pulmonary venous capillary pressure should show a *gradual disappearance* of the negative X wave between the C and V waves Unfortunately, this finding is not present constantly Also, it may be observed in mitral stenosis Right heart catheterization does, however, permit appraisal of the pulmonary vascular resistance. Frequently, the pulmonary artery pressure will be found within normal limits when measured at rest, even in patients with severe mitral insufficiency However, if the patient is made to exercise, the pulmonary artery pressure usually rises. Therefore, exercise during the right heart catheterization is essential for an accurate evaluation of the pressure in relation to the patient's routine daily activities.

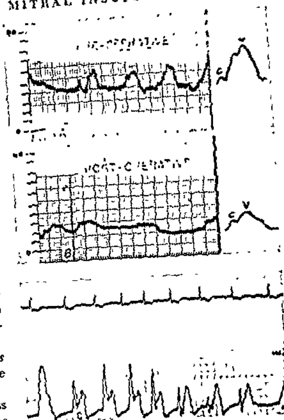


Fig. 7-60. A. *Left atrial pressure tracing in patient who had severe mitral insufficiency.* B. *Left atrial pressure tracing obtained from same patient 3 months following performance of corrective Nichols procedure. (Courtesy of Nichols. J. Thor. Surg. 1957.)* C. *Pressure tracing obtained during left heart catheterization as the catheter tip is advanced through the mitral valve orifice. Note "washing-out" of the catheter end into the left atrium due to the force of the regurgitant jet.*

The cardiac output can be calculated by right heart catheterization and is found to be *markedly reduced in* severe mitral regurgitation In 12 cases, Corlin found the cardiac *output to be* 2 5 liters/min per square meter of body *surface. In* 24 of the authors' cases, it was found to be 2 0 liters/min/square meter of body surface.

Left heart catheterization permits a more direct study of the pressure alterations within the left atrium (Fig 7-60) Certain difficulties in *differentiation* of stenosis and regurgitation are also encountered in left heart catheteriza-

insufficiency is the most frequently encountered valvular lesion. There probably are three mechanisms at play which contribute to its production. (1) There is a *dilatation of the mitral annulus fibrosus* which allows the attached leaflets to diverge. (2) There is a *loss of tone* of the ventricular musculature with consequent dilatation of the ventricular chamber. This results in a decrease in the normal sphincteric tension applied to the mitral annulus during systole by the annularly attached spiral muscles. (3) The *left ventricular dilatation (apical-basally)* is out of proportion to the length of the chordopapillary supports of the leaflets, and the resultant retraction of the leaflet edges tends to prevent systolic coaptation. With healing, a variable degree of reversal of these three factors is usual. Such patients may, in later years, develop mitral stenosis. Often an element of mitral insufficiency may persist, perhaps in combination with stenosis.

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tude of the mitral insufficiency; however, the authors have found a close *correlation* between the amount of *regurgitation* estimated from the left ventriculographic study and that found by the operating surgeon.

Ventriculography seemingly has solved the difficult clinical problem of distinction between those patients with a combination of mitral stenosis and tricuspid *insufficiency* and those with a *combination of* mitral stenosis and mitral insufficiency.

SURGERY

The variety of surgical attempts *that have* been made in recent years to restore compe- [illegible]

in overcoming this mechanical defect of the heart but also the great need that such be accomplished. The earlier surgical efforts were directed toward the objectives of placement of tissue or prosthetic devices between the leaflets, suturing of one leaflet to the other, elevation of the leaflets by stretching or cutting the chordae tendineae, or insertion of prosthetic material beneath the *mural leaflet*.

Attempts at *introducing living tissue and prostheses* between the leaflets were accompanied by a high *operative mortality and* frequently led to disappointing end results.

Suturing of one leaflet to the other failed when the leaflets were thin and pliable because they were not strong enough *to hold sutures* under tension. When the leaflets were sufficiently thickened and strong enough to hold sutures well, the stabilization *of the leaflet* edges at the point of suturing being reflected throughout the entire valve margin tended to restrict separation of the cusps and prevented descent of the leaflet edges into the left ventricle during diastole. Hence, *regurgitation was* corrected only at the expense of producing significant stenosis.

Elevation of a leaflet by chordal stretch or section has applicability only in those instances in which leaflet depression represents the entire pathologic entity. It fails to restore competence to the valve in which annular dilatation or scarring and retraction of the cusps are prominent. Division of the chordae tendineae in itself can produce severe regurgitation.

Two basic principles presently being applied surgically seem to offer *improvement* over the *previous surgical* attempts. One consists *of adding substance* to the shrunken mural leaflet in such a way as to build an extension to this *usually* immobile, nonfunctioning structure. Such an extension then can present a ledge *against which* the mobile septal leaflet can make contact during systole, thus restoring competence without producing stenosis. The second principle contemplates *bringing the existing leaflets into closer mutual proximity by alteration of the mitral annulus.*

Lillehei has applied clinically the principle of addition of substance *to the* mural leaflet. He attaches an Ivalon sponge cylinder, utilizing an *open-heart technique* (Fig. 7-61). Since the procedure is *carried* out in the collapsed and distorted open heart, it would seem that the problem *of tailoring* the prosthesis to permit exact leaflet coaptation might present some difficulties. Few cases have *been reported* in which this technique has been used, and *no* long-term follow-up is available. However, the principle appears sound, and the method might well prove a valuable addition to our armamentarium.

Alteration of the mitral ring by application *of a circumferential* suture around the entire mitral annulus has been attempted clinically by Davila et al. (1955) (Fig. 7-62), Borrie, Kent et al., and others. There is no *doubt that the regurgitation* may be effectively reduced by this procedure at the time of surgery. However, the combined *early and* late mortality *has been* high (50 to 70 per cent). *Inevitably* the constricting suture tends to cut through the soft myocardial *substance*, with loss of control of the regurgitation. Kent has reported *a* series of 33 cases operated by *the circumclusion technique*, only 11 patients now survive and only 2 *seem improved*.

Plication or distortion of the mitral annulus in such a way that that portion toward the septal leaflet side approaches that on the *mural* leaflet side has been given clinical trial by Kay, Lillehei, Nichols, and *others*. It has been carried out by closed technique, open technique, or closed technique plus utilization of partial cardiopulmonary bypass. There can be no doubt about the extreme effectiveness of this procedure at the time of surgery. The sutures can be applied selectively over the anterior or posterior pole of the valve (or both) in accordance with the localization of the re-

patient usually experiences fatigue as his first symptom and, if he continues his exertion in spite of the fatigue, dyspnea then follows. The explanation probably lies in progressively increasing pulmonary congestion as the exercise is continued, until a point is reached at which dyspnea finally appears.

Cough during rest or exercise, *orthopnea*, and *paroxysmal nocturnal dyspnea* have been present in 50 per cent of the authors' cases, while *hemoptysis* has been present in only 20 per cent.

Peripheral embolization has occurred in 8 per cent of the authors' cases and in 6 per cent in Janton's series.

Right heart failure, as a result either of a transient episode of acute left ventricular failure or of a sustained pulmonary vascular resistance had occurred in 50 per cent of the cases in the authors' series.

Signs. Of those patients who seek surgical relief for mitral insufficiency, the vast majority show a point of maximal cardiac impulse in the 6th intercostal space outside the midclavicular line, often at the anterior axillary line. The *apical thrust is usually heaving.* Occasionally a *systolic thrill* can be palpated at the apex. The heaving apical thrust can be an important sign in differentiating mitral insufficiency from mitral stenosis, in which instance a thoracic wall "shock" or "slap" may be detected.

The 1st mitral sound may be normal, decreased, or obscured by a systolic murmur In patients with atrial fibrillation, the 1st sound may be present following a short ventricular diastole and absent following a long ventricular diastole The explanation lies in the fact that an audible 1st sound indicates an area of flexibility at some point in the extent of the mitral leaflet substance Following a short period of diastole, this flexible leaflet is still depressed into the left ventricle at the time the ventricular systole forces it backward toward the atrium. As it abruptly ends its ballooning action into the left atrium, the mitral 1st sound is emitted, much as a sound is produced by a sail ballooning into a gust of wind On the other hand, after a long diastole, the mitral 1st sound is absent because the flexible mitral leaflets no longer are depressed into the left ventricle and billow more gently into the left atrium and somewhat earlier during the course of ventricular systole. The importance to be attached to the presence of a mitral 1st sound is that it indicates flexibility at some point in the valve. Such flexibility is essential if a functonal mitral valve is to be had following surgical correction.

A *systolic murmur* of at least grade III intensity is present in predominant mitral insufficiency. Usually it is a "blowing" murmur, but not infrequently a rough murmur is audible The murmur is *holosystolic:* it starts with the 1st sound often obscuring it and ends with the 2d sound. Classically, it radiates to the left axilla. However, radiation to the tricuspid area and, less frequently, to the base of the heart may occur.

A *3d heart sound,* commonly ascribed to vibration of the left ventricular wall during ventricular filling, has been frequent in the authors' previous and present series (30 per cent). If a mitral stenotic component is present, instead of the 3d sound, there may be an "opening snap." Timing is important in differentiating the etiology of the added sound An opening snap occurs closer to the 2d sound than does the 3d heart sound.[2] If some degree of mitral stenosis is present, a diastolic rumble may be audible. The 2d pulmonic sound may be normal or markedly increased in accordance with the magnitude of the pulmonary vascular resistance

If right ventricular failure occurs, engorgement of the jugular veins, congestion of the liver, and peripheral edema will ensue.

DIAGNOSTIC AIDS

Electrocardiogram. Atrial fibrillation was present in 75 per cent of the authors' cases, but even those with normal sinus rhythm showed left atrial enlargement. A normal ventricular complex was observed in 50 per cent, left ventricular "hypertrophy" in 30 per cent, right ventricular "hypertrophy" in 15 per cent, and combined ventricular hypertrophy in 5 per cent Left axis deviation and a semihorizontal or horizontal position of the heart occurred only in patients with left ventricular hypertrophy Conversely, no patient with left ventricular hypertrophy showed evidence of right axis deviation or a semivertical or vertical position.

[2] Graphic differentiation is usually easy. See Chap 9. *Editor.*

most. The usual curved posterolateral thoracic incision is made, meticulous care being taken with hemostasis. The 5th intercostal space is widely opened, and the operating table is tilted laterally until the patient is in a nearly face-down position.

The left lung is compressed posteriorly. The pericardium is incised in a line parallel to the left phrenic nerve and 1 cm posterior to it. The incised pericardial margins are retracted with weighted stay sutures. The lateral and posterior aspects of the left ventricle are inspected to determine the origin of the posterior descending coronary artery. In [illegible] it will be derived from the right [illegible] be interrupted at the site of annular plication, [illegible] this should prove unavoidable, without untoward effect since this site is close to its point of termination. However, should the posterior descending coronary branch be derived from the left circumflex artery (left coronary predominant), then it is most important that the continuity of this vessel be spared (Fig. 7-63).

The base of the left auricle is encircled with a purse-string suture of heavy (No. 2) braided silk, the ends of which are incorporated within a Rumel-Belmont tourniquet for flexible and reliable hemostasis. The auricle is clamped temporarily, and the tip is incised widely. The operator assumes a position at the opposite side of the operating table (toward the patient's face). His ungloved left index finger is inserted into the left atrial chamber as the clamp is removed from the auricle. The valve is explored digitally, especial attention being given to the size and location of the jet of regurgitation, the kind and extent of the pathologic condition of the valve, and the presence or absence of associated mitral stenosis. If significant mitral stenosis coexists, it must be relieved surgically before correction of the regurgitation is undertaken.

A very heavily fibrosed or calcified valve may prove recalcitrant to practically any corrective

Fig 7-63 Normal variations in the anatomic pattern of the coronary vessels. (*Courtesy of Schlesinger Am Asso Adv Science. 1940*) A Group I or right coronary predominant pattern (48 per cent of human cases) *In this type of heart, interruption of the terminal portion of the circumflex branch of the left coronary artery during posterior polar cross-plication of the mitral annulus fibrosus would be practically innocuous* B *Group II or balanced* circulation pattern (34 per cent of human cases) *In this type of heart, interruption of the terminal portion of the circumflex branch of the left coronary artery during posterior polar cross-plication of the mitral annulus fibrosus also would be practically innocuous.* C. *Group III or left coronary predominant heart (18 per cent of human cases) In patients with this vascular pattern the posterior descending coronary arterial branch arises from the circumflex branch of the left coronary artery. In such a case, interruption of the continuity of the left circumflex coronary branch during posterior polar cross-plication of the mitral annulus fibrosus would produce a serious injury, perhaps death The existence of this pattern of coronary distribution may be determined by inspection of the dorsal aspect of the heart prior to the passage of any plicating sutures.*



Fig. 7-61. Demonstration of mitral insufficiency by ventriculography. A Simultaneous opacification of the left ventricle and atrium which occurs in major grades of mitral regurgitation. This case was considered to represent a 3+ incompetence. B. Repeat ventriculography in same patient 8 weeks after surgical correction of mitral incompetence. Note very slight opacification of left atrium, indicating the high grade of valvular competence (*Courtesy of Nichols J. Thor. Surg* 1957)

tion[3] By the time frank "ventricularization" of the left atrial pressure curve becomes evident, the diagnosis may be made on clinical grounds alone. Comparative analysis of the contours of the pressure waves during ventricular filling does tend to differentiate mitral stenosis from mitral incompetence In mitral stenosis an AV gradient persists throughout ventricular filling, whereas in mitral insufficiency the gradient may be significant during early ventricular filling but usually disappears toward its end However, if the heart rate is rapid, there may be insufficient time for the progressive drop of the mitral gradient in mitral regurgitation to become manifest This finding of a sustained high atrial pressure during tachycardia undoubtedly helps to explain why tachycardia is poorly tolerated clinically in patients with mitral insufficiency

During left heart catheterization in a patient with severe mitral regurgitation, the catheter tip frequently will be "washed out" of the left ventricle into the left atrium during ventricular systole, returning to the ventricle during diastole. The pressure tracing then is one of alternations of ventricular and atrial pressure curves. When "washing out" of the catheter is present, it can be interpreted as good qualitative evidence of the presence of mitral insufficiency (Fig. 7-60C).

Ventriculography. Serial roentgenographic exposures following the rapid injection of a radiopaque dye into the left ventricle by direct needle puncture has been a remarkable aid in the authors' attempts to quantitate mitral insufficiency (Fig 7-61). The dye injected into the left ventricle produces varying degrees of left atrial opacification, depending upon the magnitude of the mitral insufficiency. The volume of the left atrium plays a large role in the dilution of the dye in this chamber, therefore, one must be on guard against a tendency to see a marked regurgitation when dealing with a small left atrium and a minimal regurgitation in a patient with a large left atrium Admittedly, ventriculography can offer only a gross or approximate evaluation of the magni-

[3] See Chap 13. *Editor.*

The uptake catheter of the extracorporeal circulation was inserted through a stab wound made in the outflow tract of the right ventricle, and the blood was returned to the patient by a catheter inserted into the femoral artery. Flow through the extracorporeal circulation has been as great as 3,500 ml/min The authors feel that the subtotal bypass has been of great aid as it relieves the left heart of its tension and work load during the period of definitive surgery In the absence of such bypass, the necessary manipulations of the valve may cause weak cardiac action In some cases, irreversible ventricular fibrillation has ensued. This accounted for the majority of the deaths that have occurred on the operating table With subtotal circulatory bypass, the left atrium becomes flaccid, so that its wall is easily invaginated and does not tend to tear as the annulus-piercing needles are introduced. Meanwhile, effective coronary perfusion is maintained, ensuring adequate myocardial oxygenation. After placement of a suture, the extracorporeal circulation may be slowed so that the effectiveness of the plication may be measured by the palpating finger within the atrium. The extracorporeal perfusion then can be increased if other sutures are to be applied. In the 34 cases in which the authors have utilized this method of assistance, there have been three operative deaths. Most of these were extremely bad-risk patients, and the authors believe that several more would not have survived the operative procedure had the partial bypass not been utilized.

Open Technique. The surgical correction of mitral insufficiency under direct vision utilizing total cardiac bypass is being accomplished at the authors' clinic and at many others. Not only may annular plication be accomplished, but prosthetic material may be applied to replace or reinforce the defective valve structures Although no large series of cases has been reported at the time of this writing, such will not long be the case. The inherent risks of open cardiac surgery are being mastered. For the successful correction of mitral insufficiency based upon congenital defects of the leaflets and those based upon trauma occurring during the performance of mitral commissurotomy, direct vision would seem to be a necessity.

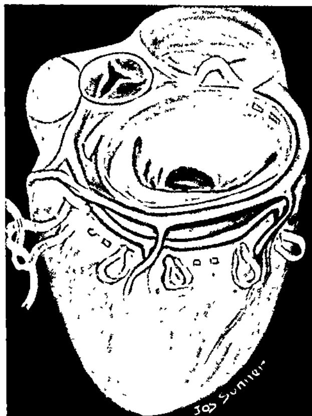


Fig. 7-62. Davila's method of encircling the mitral "annulus" with umbilical tape. *(Courtesy of Glover and Davila. J. Thor. Surg. 1957.)*

gurgitant jet. The technique is applicable to rheumatic cases regardless of the form of the underlying pathologic lesion and is ineffective only in those cases in which one of the leaflets has been divided and in those in which the septal leaflet cannot be functionally mobilized because of extreme fibrosis or calcification In some instances, the calcification may involve even the annulus or actual atrial wall.

Among the first 70 patients whom the authors operated by the *closed polar plication technique,* 40 had pure mitral insufficiency, 24 also had some element of mitral stenosis, and 6 had aortic stenosis in addition to mitral stenosis and regurgitation The ages of the patients ranged from 19 to 53. There were 19 hospital deaths (27 1 per cent) Four deaths were caused by septicemia due to antibiotic-resistant staphylococci or pseudomonas. One death was attributed to an accidental fall with head injury. One was possibly related to a technical error. In 13, death was ascribed to ventricular fibrillation, cardiac arrest, or pulmonary edema. There have been two late deaths; one, aged 53, died of hepatitis; the other, aged 52, died suddenly at home 2 weeks after leaving the hospital The authors have been impressed by the fact that the majority of deaths in their series occurred in patients over the age of 40 years.

In a recent follow-up on 40 cases 6 to 18 months postoperatively, 80 per cent were improved, 10 per cent unchanged, and 10 per cent worse.

That mitral stenosis had not been created was evident in those patients who have had postoperative left heart catheterization It is interesting that, in several cases in which a diastolic apical murmur existed preoperatively, neither this murmur nor the systolic murmur could be heard postoperatively, even though no commissurotomy was done The logical explanation would seem to be that preoperatively the septal leaflet was suspended in a relatively immobile position, a dilated annulus making traction peripherally and the tensed chordae tendineae drawing it centrally. As soon as the circumference of the dilated annulus was reduced, the septal leaflet became flaccid and was enabled to descend into the left ventricle and to fall more widely away from the mural leaflet during diastole.

This basic surgical technique has been applied in each of the authors' cases. However, the suture material used has varied. Either a heavy dacron suture or a heavy nylon suture has been used in each instance In some cases, the suture has been ensheathed with a strip of autogenous pericardium. The authors are not certain at present whether such pericardial incorporation is desirable In the laboratory animal, fusion of one site on the septal portion of the annulus to an opposing one on the mural portion of the annulus can be produced equally effectively with or without ensheathing the suture with pericardium. However, this experiment was carried out in normal dogs in which the mitral annulus was not dilated and, hence, did not impose severe tension upon the sutures. The authors' present feeling is that the bare suture is adequate. Two or more sutures should be used even though the first one effectively blocks the regurgitation. The second suture buffers the pressure on the first and permits fibrous bridging to develop between the septal annular site and that on the mural portion of the annulus.

TECHNIQUE OF POLAR CROSS PLICATION OF THE MITRAL ANNULUS FIBROSUS

Closed Technique without Bypass. The patient is positioned laterally, with the left side upper-

stone of the heart and circulation, its failure predicates irremediable disaster. Thus, again, is in contrast to the findings in mitral stenosis, where despite profound pathologic and clinical changes, even to the point of prolonged congestive failure and invalidism, the left ventricle retains its indispensable function—actual, compensatory, and recuperative—almost to the end.

Physiologically, because of the jetlike ejection of a relatively small amount of blood with each left ventricular contraction, the systolic blood pressure may not reach a high level although it is perhaps sustained and maintained longer than usual. Diastolic pressure, however, remains high, so that the pulse pressure is small and coronary artery filling, now under greater stress because of the demands of an increased myocardial mass, may be inadequate As such, these patients are often precarious anesthetic risks, to say nothing of the superimposed danger of surgery.

Clinical Correlation of Pathophysiologic Changes. To recapitulate, therefore, as a result of these pathophysiologic changes, the ultimate prognosis in a given case of aortic stenosis, almost invariably calcified and immobile, lies purely in the integrity of the left ventricular myocardium As the valve area diminishes, the increased propulsive pressure accompanying left ventricular hypertrophy is clinically manifested by forceful heart action and heart consciousness Added demands for increased cardiac output are thwarted by the unyielding valve, and fatigue and palpitation develop The left ventricular pressure rises in an attempt to overcome the obstruction, a systolic pressure of *400 mm Hg represents the extreme* in the experience of the author. Once a critical valve area is reached (approximately 0.7 cm^2 according to Gorlin), the heart is unable to maintain an adequate output. Dizziness, syncope, and precordial pain—with or without the specific changes of coronary disease—become evident. The left ventricle under these circumstances must ultimately fail, and when this occurs, disaster follows in its wake. Pulmonary congestion and edema, right heart failure, and the ever-present threat of sudden death are the consequences of this uncompensated phase of *aortic stenosis. Once this stage of diminished* cardiac output with failure of the left ventricular myocardium is reached, the prognosis becomes grave, and as a rule patients in this predicament have but a matter of months to live.

Clinical Classification of Aortic Stenosis. The necessity for translating this inexorable chain of pathophysiologic events into a reasonable, practical, clinical classification as a basis for surgical intervention is obvious. Such a clinical chain of events through which the average patient with aortic stenosis will pass is readily recognizable, although *perhaps not clearly de*fined in the mind of the physician For a number of years, the author has used a system of staging (shown in the following classification)



Fig. 7-64. A The aortic valve viewed from the aorta, showing the extremes of induration and calcification resulting in complete fixation B The same valve from the ventricular aspect.



Fig. 7-62. Davila's method of encircling the mitral "annulus" with umbilical tape. (*Courtesy of Glover and Davila, J. Thor Surg. 1957.*)

gurgitant jet. The technique is applicable to rheumatic cases regardless of the form of the underlying pathologic lesion and is ineffective only in those cases in which one of the leaflets has been divided and in those in which the septal leaflet cannot be functionally mobilized because of extreme fibrosis or calcification In some instances, the calcification may involve even the annulus or actual atrial wall.

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TECHNIQUE OF POLAR CROSS PLICATION OF THE MITRAL ANNULUS FIBROSUS

Closed Technique without Bypass. The patient is positioned laterally, with the left side upper-

tional result, in terms of myocardial efficiency, high Certainly a patient should not be allowed to go beyond stage III. Not infrequently, the patient presents himself to his physician for the first time with symptoms of dizziness, fainting, or syncope, any previous symptoms having been either mild or unrecognized Such a patient is already far advanced pathophysiologically in the course of his disease, and preparations for surgical intervention should be made without further prolonged observation and delay More often than has heretofore been appreciated *sudden death* may occur at this stage, even before signs of cardiac decompensation have developed This has been observed time and again in children under 15 suffering from the congenital form of aortic stenosis

Once compensation of the left ventricle has been broken, the mortality resulting from surgery, whatever the technique, cannot fail to rise and the ultimate clinical result is reduced Improved surgical techniques have resulted in considerable salvage of patients in stages IV and even in stage V, but postponement of surgery to this late date is not advisable These facts will become more obvious with careful study of the clinical data presented below

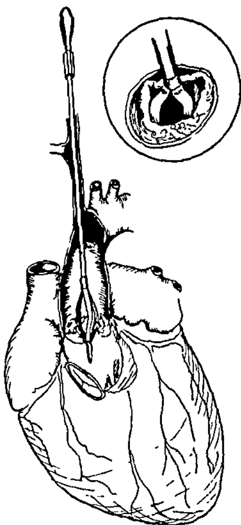


Fig. 7-66. An early approach to aortic stenosis, using the right carotid artery for the introduction of a valve-splitting instrument

HISTORY OF AORTIC VALVE SURGERY

The saga of aortic valve surgery has been sporadic One of the earliest reported approaches to this valve was by Becker, an ophthalmologist (1872) During his study of the retinal vascular changes seen in aortic insufficiency, he lacerated the aortic leaflets in animals, employing a glass rod passed down through the carotid artery into the ascending aorta Similarly, in 1907, Harvey Cushing produced aortic regurgitation, using a valvulotome (Fig 7-66) Tuffier (1913) is credited with the first direct attack on aortic stenosis in a patient Although he proposed to incise the stenotic valve in a 36-year-old subject, at the time of surgery he was satisfied to invaginate the aortic wall into the valve orifice manually The patient survived this procedure. In the light of present knowledge, it is hard to conceive that this method could have effectively relieved much of the stenosis encountered. Brock (1947) visualized the aortic valve through the right subclavian artery, using a specially designed cardioscope His intent was to relieve the aortic stenosis by direct instrumentation, but after seeing the irregularly calcified valve, it seemed obvious that direct valvotomy could not be carried out without undue risk A major impetus to aortic valve surgery was provided by Smithy, who himself suffered from the ravages of the disease he hoped to be able to control He concluded from his experimental work that the transventricular route to the aortic valve was preferable Interestingly enough, he also chose this same approach to the mitral valve

Experimental studies reported by Bailey, Glover, O'Neill, and Ramirez (1950) included attempts to replace the valve by grafts, bypass procedures to circumvent the aortic valve, backward cutting punches to open the valve commissures, and various modifications of direct valvular incision, as suggested by the work of Brock with regard to pulmonary valvotomy Direct-vision replacement of stenotic valves using a baffle clamp was reported by Litwak et al. (1952). In 1953 Daniel and Scott attempted to open stenotic aortic valves in three patients by direct insertion of a finger through

measure. Fortunately, in most cases of severe mitral regurgitation, at least the septal mitral leaflet will be found to be relatively thin and flexible, thus offering valve mobility and function provided that the disparity between the amount of available leaflet substance and the size of the AV channel can be overcome. In the vast majority of patients, the regurgitant jet will be localized to the posteromedial portion of the valve aperture.

Having decided that this is the case and that the technique of plication of the annulus fibrosus in the region of the posterior pole of the valve is applicable, a heavy suture of braided nylon or orlon with a large curved needle swedged at either end is selected. The point of one of the needles is caused to penetrate the left atrial chamber at a site well posterior to the medial portion of the annulus fibrosus and close to the atrial septum. It is well to place a mattress suture of No. 0000 silk in the atrial wall about the site of puncture to guard against the possibility of serious bleeding during further manipulations of the needle. With guidance of the intracardiac finger, the needle point is advanced until it can be directed beneath or around the medial portion of the annulus at the selected level Because of its curvature, the needle tends to return to the left atrial chamber, assisted by depression of the septal valve leaflet with the intracardiac fingertip Further passage of the needle causes it to follow its natural arcuate course and to emerge from the left atrial wall The needle is drawn completely out of the heart, and another mattress suture of No 0000 silk is placed about the site of emergence to prevent bleeding. The patient is permitted to rest for a few minutes to ensure recovery from any disturbance to cardiac function which may have been induced by the intracardiac manipulations

Now the needle is grasped in a reversed manner by the holder and is reintroduced into the left atrial chamber *exactly* through the site of emergence. Should the suture subsequently be found to be "hung up" by a few fibers of atrial wall because of inexactness in reentry, they may be broken by intracardiac digital manipulation The needle point is directed in such a way that it passes beneath the mural portion of the annulus fibrosus at a point deemed to be opposite to that encircled upon its medial portion Continuation of its arcuate passage causes the needle to emerge from the left ventricular wall close to the AV groove Again the heart is afforded an opportunity to recover from any disturbance incident to the procedure

Now the needle on the trailing end of the suture is guided into the left atrial chamber, passing exactly through the site of initial entry. It is so directed that it pierces the lateral atrial wall from within at a site just above the mural portion of the annulus fibrosus which corresponds to the final exit of the leading end of the suture. This is readily discernible to the intracardiac finger. The contents of the AV groove are elevated by retraction with the extracardiac hand in order to elevate the left circumflex coronary artery from the underlying annulus fibrosus, thus making it easier for the needle to pass between this fibrous ring and the artery. However, as mentioned previously, if the pattern of the vascular anatomy is of the usual right predominant form, no harm would result if the left circumflex coronary artery were to be included inadvertently within the suture (Fig 7-63).

An assistant now advances the needle which emerges from the left ventricular wall close to its fellow. Again a few mintues of rest are allowed for the circulatory status to become stabilized.

When deemed necessary, a second or even a third plicating suture may be applied at once. Care then must be taken not to confuse or entangle the multiple sutures. Usually it has been the authors' custom to tie each suture down as soon as placed, thus affording the patient the advantage of improving valve function as the surgery progresses.

In most cases, a small pledget of Ivalon (formalized polyvinyl plastic) sponge is impaled upon the suture ends before tying down. After tightening the first throw of the knot, a small clamp is applied to hold its position. Five or ten minutes of rest is permitted Not only is the circulatory status thereby stabilized, but any soft tissue included within the loop of the suture will become "cut through" during this period, tending somewhat to loosen the tension of the knot.

The clamp is removed, and the knot is further tightened and then is tied down permanently Evaluation of the regurgitant jet by the intracardiac finger will disclose the effectiveness of the procedure However, even if all the regurgitation has been abolished by the first suture, it is the authors' policy to place and tie at least one more at a more central site. Care must be taken that any such additional "electively" applied sutures do not reduce the effective valve aperture significantly.

Should the regurgitant jet have been localized in the region of the anterolateral valve pole, an appropriate anterior polar plication would have been performed

Closed Technique with Bypass Assistance. In their last 34 patients, the authors have utilized partial cardiopulmonary bypass as an adjunct to the closed operative technique. The definitive procedure is similar to the former one.

by Brock, was employed for the remaining 41 patients, operated on since 1955. This instrument is light but exceptionally strong, is no larger in caliber than the usual lead pencil, and its expansible head is equipped with two parallel blades rather than three as were formerly used. It does not cut but dilates the valvular orifice to cause splitting of one or two commissures, occasionally three.

Briefly the technique employed is as follows: a left posterolateral approach is used, entering the pleura through the widely opened *5th interspace*, giving excellent exposure to the left ventricle and indeed the entire left heart. The pericardium is opened vertically, anterior and parallel to the phrenic nerve from the level of the aortic arch to the diaphragm, thus widely exposing *the left heart* and great vessels. The aortic *ring* and its contained valvular tissues are explored externally by palpation, and in most instances considerable information regarding the type of valve to be encountered, including the degree of calcification and its involvement of the surrounding aortic wall or myocardium, can be gained. The ascending aorta is likewise palpated for an estimation of the degree of thrill present and the extent of the poststenotic dilatation of that structure.

Direct pressures are taken from within the ascending aorta, the left ventricle, and the left atrium. The systolic aortic gradient indicative of a block has ranged from 30 to 250 mm Hg in this series. Some authors feel that the measurement of these pressures under anesthesia and in the open chest in this manner is of little value and is not an accurate hemodynamic measurement. While this may be true in the strict academic sense, for practical purposes, these measurements are of the greatest value for, not only do they give one an estimation of the degree of block but, by comparing pre- and postcommissurotomy pressures, very definite knowledge of the efficiency of the procedure performed can be obtained. *Indeed most* of the pressure tracings taken in this manner agree amazingly closely with those taken by left heart *catheterization prior to surgery, so that the* author believes that this type of hemodynamic control is absolutely essential to the proper performance of aortic valve surgery.

A *Statham* P 23 D transducer, *using an atmospheric* O point, is the type of gage employed (Fig 7-68). The head vessels are not isolated or constricted in any manner during the operative procedure. In the experience gained from over 1,000 mitral commissurotomies, no *diminution in* the incidence of cerebral emboli could be recognized between those patients who did not have temporary occlusion of these arteries and those in whom this measure was employed. Indeed, the *author feels that such a measure* is more dangerous than no occlusion at all. Strangely, although one would expect a much higher incidence of emboli in aortic stenosis where the valves are almost routinely heavily calcified, embolism in the *author's experience* following aortic commissurotomy has been rare, considerably less than that seen in mitral commissurotomy.

A 1-cm incision halfway through the thickened

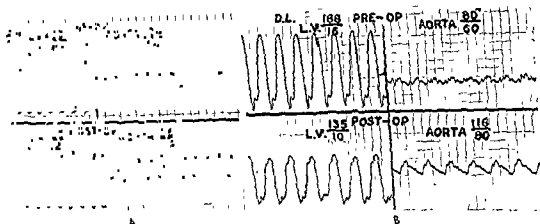


Fig. 7-68 A Pre- and postaortic commissurotomy pressure tracings taken within the left ventricle and aorta. Note the highly satisfactory *reduction* of the aortic valve block (from 94 mm Hg to 4 mm Hg). B Typical hemodynamic response within *left ventricle* and aorta to *transventricular* aortic commissurotomy by the method described

1

Surgery of aortic stenosis

ROBERT P. GLOVER

The problems associated with the surgical alleviation of aortic stenosis have to date presented far greater difficulties than any of the other stenotic valvular lesions That this is true has been recognized since the first surgical attempt to relieve an obstructed aortic valve (Tuffier, 1913). The exact nature of these difficulties, however, has only been fully appreciated within the past decade, during the recent renaissance of intracardiac valvular surgery. Although as much if not more time and valiant effort, both experimental and clinical, has been directed toward the relief of this most intractable of valvular lesions, as compared to tricuspid, pulmonary, and mitral stenosis, equal success has not as yet been forthcoming There are a number of reasons for this state of affairs.

Pathophysiologic Changes. *Anatomically,* the valve is the least accessible to exploration, for it lies centrally placed within the confines of the heart. The left ventricular myocardium is invariably hypertrophied to a considerable degree. This finding, together with the tremendous vascular pressure generated within its outflow tract, prevents the use of an immediately subaortic transmyocardial incision for the insertion of the finger or instrument, similar to that used in pulmonary valvotomy, because uncontrollable hemorrhage will surely follow. The valve cannot be effectively reached through an auricle. The position of the ostia of the coronary vessels lying directly behind the valve leaflets makes direct reconstructive surgery hazardous. An approach from above directly through the aortic wall presents the same difficulties encountered in the immediate subaortic transmyocardial approach. Thus, definitive technical approach to the valve is unfavorable.

Pathologically, there is an early fusion of the three valve cusps, the margins of which become thickened, rolled, and infiltrated with calcium very early in the course of the disease. This is due in part to the underlying disease itself but also, and perhaps more particularly, to the location of this valve in the course of the blood stream The valve lies in a confined space of small diameter and is the recipient of the full head of vascular pressure from the strongest of the contracting cardiac chambers, the left ventricle. The factor of vascular trauma is, therefore, of great importance for, following initial fibrotic agglutination of the cusp margins, there is a constant and steady deposition of elements, such as fibrin and calcium, from which there can be no relief. Thus, calcification develops early, and as the leaflets are relatively small in surface area, almost complete immobility and fixation may rapidly eventuate (Fig. 7-64) Some flexibility of the cusps at their attachment to the aortic ring may remain for a time, but this is less prominent than that seen in the stenotic mitral valve This factor of trauma no doubt partially explains the fact that the anteromedial leaflet of the mitral valve, also called the aortic or septal leaflet, is the seat of the greatest calcification in mitral stenosis, for it lies nearest the aortic ring in the left ventricular outflow tract, a zone of high pressure, and also receives the brunt of vascular ejection at the time of left ventricular contraction. Therefore, from a pathologic standpoint, surgical intervention in aortic stenosis, effectively to restore a measure of normal valve leaflet motion, must be carried out before extremes of the above-described process are reached. To wait longer merely compounds the likelihood of surgical failure, for, in consequence of the valvular change, the left ventricular myocardium hypertrophies and dilates, in due time to wear out and become incapable of effective action As the left ventricle is the corner-

by Brock, was employed for the remaining 41 patients, operated on since 1955. This instrument is light but exceptionally strong, is no larger in caliber than the usual lead pencil, and its expansible head is equipped with two parallel blades rather than three as were formerly used. It does not cut but dilates the valvular orifice to cause splitting of one or two commissures, occasionally three.

Briefly the technique employed is as follows. A left posterolateral approach is used, entering the pleura through the widely opened 5th interspace, giving excellent exposure to the left ventricle and indeed the entire left heart. The pericardium is opened vertically, anterior and parallel to the phrenic nerve from the level of the aortic arch to the diaphragm, thus widely exposing the left heart and great vessels. The aortic ring and its contained valvular tissues are explored externally by palpation, and in most instances considerable information regarding the type of valve to be encountered, including the degree of calcification and its involvement of the surrounding aortic wall or myocardium, can be gained. The ascending aorta is likewise palpated for an estimation of the degree of thrill present and the extent of the poststenotic dilatation of that structure.

Direct pressures are taken from within the ascending aorta, the left ventricle, and the left atrium. The systolic aortic gradient indicative of a block has ranged from 30 to 250 mm Hg in this series. Some authors feel that the measurement of these pressures under anesthesia and in the open chest in this manner is of little value and is not an accurate hemodynamic measurement. While this may be true in the strict academic sense, for practical purposes, these measurements are of the greatest value for, not only do they give one an estimation of the degree of block but, by comparing pre- and postcommissurotomy pressures, very definite knowledge of the efficiency of the procedure performed can be obtained. Indeed most of the pressure tracings taken in this manner agree amazingly closely with those taken by left heart catheterization prior to surgery, so that the author believes that this type of hemodynamic control is absolutely essential to the proper performance of aortic valve surgery.

A Statham P 23 D transducer, using an atmospheric O point, is the type of gage employed (Fig. 7-68). The head vessels are not isolated or constricted in any manner during the operative procedure. In the experience gained from over 1,000 mitral commissurotomies, no diminution in the incidence of cerebral emboli could be recognized between those patients who did not have temporary occlusion of these arteries and those in whom this measure was employed. Indeed, the author feels that such a measure is more dangerous than no occlusion at all. Strangely, although one would expect a much higher incidence of emboli in aortic stenosis where the valves are almost routinely heavily calcified, embolism in the author's experience following aortic commissurotomy has been rare, considerably less than that seen in mitral commissurotomy.

A 1-cm incision halfway through the thickened

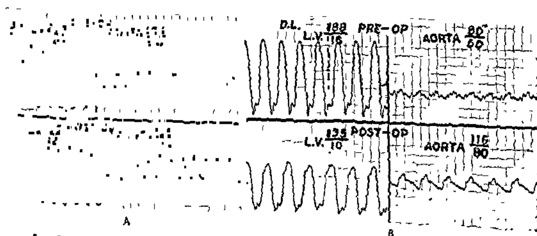


Fig. 7-68. A Pre- and postaortic commissurotomy pressure tracings taken within the left ventricle and aorta. Note the highly satisfactory reduction of the aortic valve block (from 94 mm Hg to 4 mm Hg). B Typical hemodynamic response within left ventricle and aorta to transventricular aortic commissurotomy by the method described.

CLINICAL CLASSIFICATION OF AORTIC STENOSIS

Stage	*Symptoms*
	Before left ventricular failure:
I	Asymptomatic; murmur only
II	Fatigue, heart consciousness, palpitations
III	Syncope and/or angina; reduced cardiac output
	After left ventricular failure:
IV	Episodic pulmonary congestion
V	Frank congestive failure

so that, when the afflicted patient comes for evaluation, some estimation of his status in relation to the timing of possible surgical intervention can be made. In this way, it is almost immediately possible, within reason, to recognize just where the patient may be in the overall course of his disease syndrome. Thus, the patient can be more intelligently managed

Stage I is that period during which the typical systolic murmur of aortic stenosis is present, but before subjective symptoms have resulted. *Stage II* marks the onset of an ill-defined period in which the patient becomes subjectively aware of his forceful heart action (palpitation), easy fatigue becomes noticeable, and his attention may be called to the unusual visible pulsations in his supreclavicular areas and at the suprasternal notch Admittedly, this stage is not specifically characteristic of aortic stenosis per se, but when seen in the patient whose cardiac changes are those of aortic stenosis, the combination of the valvular changes and symptoms takes on added significance. It is an indication that the myocardium is beginning to feel the effects of an unyielding obstruction at the aortic valve level. *Stage III* ushers in the obvious period of progressive disability due to a diminishingly effective cardiac output, evidenced by episodes of dizziness or syncope or by substernal discomfort, tightness, and exertional pain, indicative of an inadequate coronary flow (Fig 7-65). With beginning left ventricular failure, *stage IV* is characterized by episodes of pulmonary congestion and edema, at first rather easily controlled by medical measures, but shortly to become refractory to even the most vigorous management. *Stage V* connotes impending disaster and an early demise, for in addition to left ventricular failure, superimposed right heart failure with hepatomegaly, ascites, and peripheral edema now labels the heart picture as one of almost irretrievable damage not to be reversed by any regime, medical or surgical

With such a progression of easily recognizable clinical findings, it becomes obvious that, if surgery is to be of any real benefit, it must be performed at a time when the left ventricle is still intact. Ideally, therefore, *the patient in stage II would represent the best candidate, for the mortality will be low and the func-*



Fig. 7-65. Typical cardiac configuration in aortic stenosis before onset of left ventricular failure. Note enlarged left ventricle and ascending aorta.

completely. When the hopeless nature of the pathologic process is fully appreciated, it will be recognized that the *surgeon is attempting merely to improve flow to a maximum degree and not to restore the valve or its action to a normal state, which is obviously impossible*. Most valves in acquired stenosis have lost all semblance of a valve for there is little if any pliability to assure valve action. One is, therefore, attempting to provide an *increased orifice* with the hope that some measure of valve motion may be restored, depending upon the individual nature of the particular patient's condition. No more than this can be expected until it will be possible to resect the entire calcified structure and replace it with a suitable prosthesis.

The tiny myocardial wound is reinforced with two or three heavy sutures, the pericardium is closed completely, having placed a dependent incision posteriorly for drainage into the pleural space. The chest is closed in the usual manner, using catheter drainage of the pleural space routinely.

In patients whose myocardium has deteriorated to an exceptional degree or in whom precordial pain is a prominent preoperative symptom, a second intervention can be done: the internal mammary artery is divided from within the left chest at the level of the 2d anterior interspace, and after the chest is closed and the patient is placed on his back, the right internal mammary artery is also divided through a small secondary incision. This feature has been added because of the marked symptomatic improvement obtained in many patients suffering from precordial pain due to coronary insufficiency, when this procedure has been employed.

HEMODYNAMIC OBSERVATIONS

In this series of cases, cardiac and arterial catheterizations were carried out preoperatively in 47 instances. When possible, and this was accomplished not infrequently, the arterial catheter placed into the arch of the aorta was passed retrogradely across the aortic valve into the left ventricle.

For an accurate evaluation of the severity of aortic stenosis, left heart catheterization is essential, either by the retrograde aortic method as suggested above or by direct puncture of the left atrium or ventricle. Only in this way can a true measure of valvular obstruction preoperatively be obtained and the proper course of action verified.

Aortic and brachial artery pressure tracings, routinely taken, show contours suggestive of

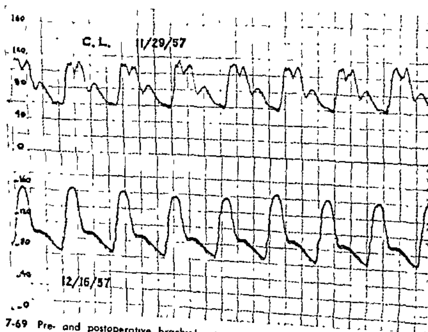


Fig. 7-69 Pre- and postoperative brachial artery tracings showing improvement after aortic commissurotomy

the myocardium of the outflow tract of the left ventricle, but none of these patients survived.

Sarnoff and Case (experimentally) used plastic valves of the Hufnagel type interposed between *the left ventricular apex and the aorta to bypass* the aortic valve, but the high incidence of erythrocyte destruction and resultant emboli precluded clinical trial. Plastic and tissue diverticula sutured to the aortic wall just above the valve area have been used as tunnels to permit digital palpation and manipulation of the valve (Fig. 7-67A). Glenn, Bailey, Swan, and Harken have expressed enthusiasm for this approach. Open cardiac surgical procedures employing *hypothermia* or extracorporeal bypass have received considerable attention *in recent years* Valuable *contributions to this* aspect of the problem have been made by Swan, Lewis, and Lillehei. Whereas this approach may *ultimately be of considerable value in the congeni*tal forms of aortic stenosis when employed at an early age, it would seem to have little place in the surgery of acquired aortic stenosis until such a time as it becomes feasible totally to resect the damaged valve and replace it with a plastic prosthesis.

Transventricular Approach to Aortic Stenosis. Despite the many ingenious approaches outlined, the author has been convinced from the inception of modern valvular surgery that, until hopelessly diseased and distorted aortic valves can be removed and replaced with *impunity, the best functional result with the low*est risk to the patient will be obtained using *a properly performed transventricular route.* To support this contention, a consecutive series of 78 cases is presented, representing the two phases of transventricular commissurotomy techniques through which the author has passed. This *series* was begun 1951 and includes every patient operated on through June, 1957.

The age range in this group was from 4 to 57. In 24 of these patients, combined mitral and aortic *commissurotomies* were performed. In one instance, an associated coarctation of the aorta was resected with end-to-end anastomosis after the aortic commissurotomy was *accomplished* The great majority of these operations were carried out in patients in the far-advanced stages of their disease. Of the 78 patients, 70 had moderate to *marked* calcification of the aortic valve. There were 13 in permanent atrial fibrillation (10 of them were suffering from both mitral and aortic stenosis)

The first 37 cases in this series were operated on by the technique reported in 1952, employing a large three-bladed expansible split-dilator (Larzelère—Donaldson design) inserted through a widely purse-stringed avascular area near the apex of the left ventricle (Fig. 7-67B). This method has long since been abandoned because of the un*wieldiness* of the instrument, the unnecessary myocardial trauma, and the excessive blood loss which it occasioned. A more refined technique using a dilator (*Fig* 7-67C) demonstrated to the author

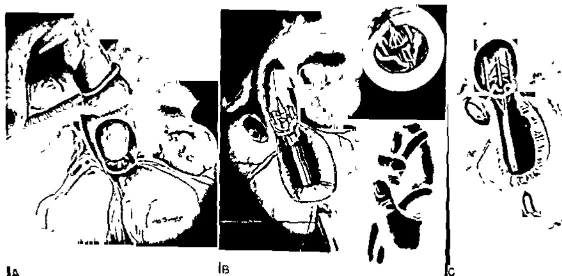


Fig. 7-67. A. Approach to the aortic valve through the aorta itself, employing a plastic sleeve suture to the aortic wall for the insertion of the exploring finger and instrument. B. The original large-sized three-bladed aortic valve dilator for transventricular approach to the valve. Note guide wire in the aorta over which the instrument is threaded and the wide myocardial purse string employed for hemostasis during manipulation. C. The small but powerful two-bladed dilator presently used for the transventricular approach.

TABLE 7-11. ANALYSIS OF LATE DEATHS FOLLOWING AORTIC COMMISSUROTOMY

Stage	No. of cases	Survival period, months	Cause of death
		Old technique	
II	1	10	Subdural hematoma
III	4	5	Congestive heart failure
		24	Congestive heart failure
		17	Congestive heart failure
		35	Coronary occlusion
IV	1	8	Sudden collapse
V	3	36	Suicide
		41	Congestive heart failure
		5	Pulmonary embolus
		New technique	
III	2	12	Congestive heart failure
		7	Congestive heart failure with aortic insufficiency
IV	3	9	Suicide
		14	Congestive heart failure
		1	Congestive heart failure with aortic insufficiency
V	2	4	Active rheumatic heart disease with bacteremia
		2	Cardiac arrest
	16	1–41	

tient has occasional dyspnea on exertion, and another takes infrequent nitroglycerin tablets for chest pain but otherwise remains improved

Of the 41 patients operated upon by the new technique (1955 to 1957), 33 have been analyzed, there being a reasonable length of observation of a year or more. Of these patients, 25 are alive and 22 are very definitely improved These have shown definite symptomatic improvement and, in them, again surgery has been of great benefit. To be sure, these patients realize that they do not have new hearts or new valves, but they are now living with their diseased condition in a vastly improved state still requiring careful medical observation and management None of this group has shown signs or symptoms of aortic insufficiency A total of 19 have returned to various degrees of work, ranging from housework to welding The incidence of syncope, dizziness, shortness of breath, chest pain, orthopnea, and recurrent congestive failure has been uniformly improved or, in most cases, abolished Thus, 22 of the 33 patients in this newer group have been materially helped by surgery (67 per cent). The remaining 8 patients of the new group of 41 are all living and improved within the first year, but not enough time has elapsed to include them in the larger group of late results.

Three of the patients in the newer group have not been benefited although they are still alive. One is the patient operated upon for erroneous diagnosis proved at operation to be that of idiopathic hypertrophy of the left ventricle without valvular involvement. Another patient, although able to work intermittently, is orthopneic, has angina and dizziness, and is unable to climb stairs. The third, while improved from the cardiac standpoint, is still recuperating from an operative cerebral embolus.

DISCUSSION

It is felt that the technique presented by the transventricular route is far and away the best

TABLE 7-12 LONG-TERM RESULTS FOLLOWING AORTIC COMMISSUROTOMY

Stage	No of cases	Survival period, months	Present status
		Old technique	
II	2	32, 57	Improved
III	4	38–63	2 Improved 2 Excellent
IV	4	37–64	Improved
V	1	47	Improved
	11		
		New technique	
II	1	16	Excellent
III	13	8–31	5 Excellent 7 Improved 1 Unimproved
IV	9	9–22	3 Excellent 5 Improved 1 Unimproved
V	2	10–27	Improved
	25		

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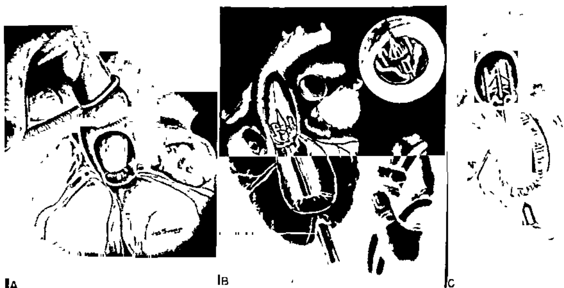


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V	2	10–27	Improved
	25		

left ventricular myocardium so as not to enter the lumen is made in an avascular area near the apex of the left ventricle. No bleeding results from this initial incision. No purse-string and no stay sutures of any type are used for they tend to damage or crush the myocardium or often pull out, with resultant laceration of this muscle. With this technique, bleeding is so minimal that such measures are not needed. It is vital to recognize this fact for it is one of the major refinements responsible for present improved mortality statistics. At this point, all is in readiness for the passage of the aortic dilator. The second major feature in this improved technique occurs at this point. All operative manipulation ceases, and for 5 min by the clock the anesthetist completely expands the lungs and oxygenates the patient to the fullest. It is felt that this lowers the possibility of myocardial ischemia and resulting arrhythmias during the period of manipulation; since observance of this feature, arrhythmias other than an occasional premature contraction have rarely been seen.

Exposure is then obtained, and the two-bladed Brock dilator is gently pressed into the previously initiated incision. As the myocardium contracts and relaxes, the dilator held against it with slight pressure dissects its own way through the myocardium into the lumen of the left ventricle. The dilator is then guided upward and passed through the stenotic aortic orifice, being aided in this maneuver by the external hand which is placed about the aortic ring as a target at which to aim. The entire passage of the instrument is done slowly and with deliberation and in a very gentle manner so that there is no jabbing or thrusting under pressure. It is important to realize that the initial passage toward the aortic valve is downward toward the floor, rather than immediately upward toward the head. This point might be forgotten in the excitement of the operative maneuver. To direct it immediately upward is to impinge upon the interventricular septum or myocardium, leading to injury or arrhythmia. A few seconds may be necessary to find the exact orifice for often one impinges upon exuberant calcified plaques and induration occurring in the outflow tract just proximal to the valve or which may be protruding down from the valve itself like thickened stalagmites. With care and deliberation, there has been no instance in which the valve orifice could not easily be entered. The hand (left) which is palpating the aortic ring externally can appreciate the presence of the dilator within the orifice and can feel half of the dilating head extending out into the aorta itself.

When the dilator is properly placed, it is slowly opened to its full extent, first in one plane, and then is carefully rotated in two other planes to ensure the maximum separation of fused valve elements at the commissures. No attempt is made to recognize anatomically each commissure for these valves are so badly diseased and distorted that such recognition is impossible. The dilator is merely opened where it will in the three planes mentioned, and routinely the fused valve cone will split at its commissures. One and usually two commissures are readily opened in this manner, occasionally three, although this is unusual. One can feel the valve split and crunch as its calcific fusion is split asunder. It is the source of utter amazement to the author that all these patients do not suffer clinical emboli at this time, for without question innumerable sandlike particles are dispersed into the circulation, but, as stated above, evidence of clinical emboli during the postoperative period is rarely seen. Should the head of the dilator be felt to slip upward into the aorta or backward into the ventricle because of the toughness of the tissues, thereby modifying the splitting compression, the maneuver is repeated rapidly at two or three levels along the outflow tract or up in the aorta to ensure maximum separation of valvular elements. The instrument is closed and slowly withdrawn. Pressure over the small linear 1-cm incision with the finger and a sponge for 1 or 2 min will in almost every instance cause complete cessation of bleeding, and with careful manipulation, the tiny incision has not been enlarged upward or downward, so that an absolute minimum of myocardium will have been injured.

When the heart rate and action are stable and the blood pressure has returned to the same level as it was prior to commissurotomy, the pressure measurements are repeated in the aorta, left ventricle, and left atrium. In most instances, the gradient will have dropped dramatically. In others, it will not seem to be entirely effective, so that the dilator may be introduced again, two, three, and even four times, for it is well tolerated as a rule. Occasionally, the head of the dilator is removed and another of the same design but larger is attached, a modification of Brock's instrument. This has been effective in further reducing the gradient. In many instances, the gradient has been all but abolished, and in many others has dropped to less than 30 mm Hg (Fig. 7-68B). One must remember that often it is impossible completely to abolish the block at the aortic valve level purely because of the physical presence of large amounts of calcium, whose presence at this location precludes such an accomplishment. Such valves cannot retract or open

17

Surgery of aortic valvular disease[1]

CHARLES A. HUFNAGEL AND PETER W. CONRAD

The development of satisfactory direct methods for the correction of lesions of aortic stenosis and aortic insufficiency has led to a marked improvement in the ability of the surgeon to offer a solution of these problems

Four prime requisites must be fulfilled before the problems of the direct reconstruction of the aortic valve and ascending aortic arch can be met satisfactorily (1) a safe and reliable extracorporeal circulation system, (2) a method for the bloodless isolation of the aortic root, aortic valve, and left ventricular outflow tract, (3) an adequate understanding of the pathologic alterations of the underlying causes

[illegible] prosthesis for the replacement of all or any part of the aortic valve that may be functionally destroyed Currently, all these criteria can be met at a high level of predictability

Extracorporeal circulation[2] has become, in experienced hands, such a highly satisfactory technique that further comment is not indicated The use of this method *in conjunction with controlled body temperature*[2] has been a major advance in the general method The incorporation of a heat exchanger into the apparatus permits one to regulate the temperature accurately and rapidly at any desired level. The reduction of body temperature permits more adequate perfusions under difficult technical conditions than would otherwise be possible It is sometimes helpful to reduce the total body temperature to below 10°C in order to be able to interrupt total perfusion for brief periods of time. This is rarely necessary in the patient with aortic valvular disease, but it offers an additional safeguard under unusual circumstances and it can be helpful in the induction of cardiac arrest.

All operations upon the aortic valve are now done under direct vision.

To gain access to the aortic root, one must isolate the area of the ascending aortic arch which bears the origin of the coronary arteries, in order to render it bloodless for the period of the procedure. This may be achieved by clamping the ascending aorta at the level just proximal to the brachiocephalic artery. Cardiac metabolism must be reduced to a point at which total lack of coronary perfusion can be tolerated for the required period, or else the coronary arteries must be perfused. For the past 2 years the authors have used local cooling to produce *cardiac arrest* The myocardial temperature is lowered to approximately 10°C and maintained at that level throughout the procedure Cardiac arrest occurs promptly and is maintained throughout the operation. Following closure of the aorta, the coronary flow is again restored. The heart is defibrillated, and then it resumes a normal sinus rhythm. Venting of the left side of the heart during the period of restoration of the normal mechanism is essential This method gives a safe period of up to at least 90 min for the completion of the

[1] This new chapter of Drs Hufnagel and Conrad represents a great step forward in the surgical treatment of aortic valvular diseases The previous chapter (Surgery of Aortic Stenosis) is actually superseded by this new chapter because aortic commissurotomy is gradually being replaced by aortic valve replacement. Chapter 18 of Part 7 is temporarily left in the volume because of its historical value *Editor.*

[2] See also Part 0, Chap 16 *Editor*

aortic stenosis, with a typical curve indicating a delayed and notched ejection phase (Fig. 7-69). Cardiac outputs (Fick) varies from 2.10 to 5.96 liters/min, averaging 3.77 liters/min for the catheterized series.

Since 1954, direct-pressure studies have been routinely made at the time of surgery. The precommissurotomy systolic gradients across the aortic valve have varied from 8 to 250 mm Hg, averaging 78 mm Hg. (The patient having only an 8-mm gradient was operated upon by mistake for, although her studies and symptoms were characteristic of aortic stenosis, at operation she proved to be suffering from idiopathic hypertrophy of the left ventricle without valvular component.) Postcommissurotomy aortic valve gradients range from 0 to 75 mm Hg, averaging 29 mm Hg.

A slightly greater hemodynamic change occurred in the patients who had not gone into failure prior to surgery Of 19 patients in stage II or III having operative pressure studies, the left ventricle–aortic systolic gradients averaged 83 mm Hg before and 29 mm Hg after commissurotomy, a reduction of 54 mm Hg, obviously of marked significance. The average systolic gradient in 24 patients in stages IV and V (after left ventricular failure) dropped from 70 mm Hg to 28 mm Hg following commissurotomy (a 42-mm reduction)

It is obvious that complete abolition of the valvular gradient rarely occurs, for reasons considered above, namely, the nature of the process These hemodynamic results are an improvement over those which have been published (very few reported) by all other aortic valvular approaches.

MORTALITY

It is the firm conviction of the author that, until the aortic valve can be replaced, the transventricular approach properly employed is a safe and effective method for the relief of aortic stenosis.

As yet no appreciable series of extracorporeal methods for the relief of acquired aortic stenosis have appeared in the literature, but in the few small series reported the mortality rate has ranged from 50 to 100 per cent. This obviously represents a developmental phase which should be short lived once adequate valvular replacement becomes possible. In the recent past, Bailey reported an operative mortality of 15.1 per cent using the aortic approach to the valve, but few have attained these results. On the other hand, Brock's success with the transventricular route has been very impressive. His over-all operative mortality has been 16 per cent, but in his most recent reports (63 cases), there were but 4 deaths (6 per cent mortality).

The deaths in the author's series of 78 patients are divided into two categories.

Operative Deaths. These include patients who died in the hospital during surgery or up to 1 month later. Among the 37 patients operated on by the older technique, there were 17 deaths (a mortality of 46 per cent, obviously intolerable). In the more recent group of 41 patients operated on by the present technique (outlined above), there have been but 2 deaths (a mortality of 4 9 per cent).

In both groups, 17 of the 19 operative fatalities were in patients in the late stages of their disease, having been in repeated cardiac failure (stages IV or V), and 13 were in stage V. There were 13 deaths of cardiac origin; the remainder occurred during the postoperative hospitalization from congestive heart failure (3), myocardial infarction (1), operative embolus (1), and cerebral vascular accident occurring 10 days postoperatively (1).

Late Deaths. In the entire series, 16 patients died after leaving the hospital (1 to 41 months after surgery). Of these late deaths, 9 occurred in patients who had been subjected to the old operative technique, 7 were in the group who underwent the new operative technique These data are presented in Table 7-11. It should be added that 2 of the patients who died at a late date after surgery did not die from their cardiac disease per se for they committed suicide. Each of them had obtained a good functional result but lived in fear and dread of their disease potential and could no longer face reality because of this fear.

Although many of these patients have died in various parts of the country, nevertheless autopsies have been obtained in 16. Coronary occlusion was demonstrated in 2 of them. The coronary arteries were patent in the remaining, although some evidence of atherosclerosis was as a rule observed.

CLINICAL RESULTS

The present status of patients presently living has been ascertained either by direct examination or from specific reports by the referring physicians Of the 37 patients operated upon by the older technique, 11 are living (2½ to 7 years) and all are distinctly improved (Table 7-12). Their ability to work, walk, and indulge in mild exercise is better than it had been at any time during the years immediately before surgery so that for them the operation was well worth while One pa-

pertrophy are not advised to have operation, although the authors have recently modified and improved a procedure which they had previously devised with the hope that it may be useful in these cases. They anticipate that this method will be employed in the near future.

In patients with *acquired valvular obstruction*, the onset of *syncope*, precordial pain, or a change in the patient's exercise tolerance are strong indications for operation. The onset of *signs of heart failure*, which may be evident only on close study of the patient, or the development of increasing heart size or evidences of left ventricular overload are also indications for operation when it can be demonstrated that there is a high degree of obstruction Patients who are under observation because there has not yet been sufficient evidence of serious obstruction to warrant surgical intervention must be watched carefully for signs of progression Evidence of progression in such patients, either by signs or by symptoms, is an indication for operation Patients who manifest conduction defects or suffer from congestive failure, which is extremely difficult to control, carry a higher risk than other groups Left ventricular impairment due to advanced disease constitutes a major hazard to satisfactory recovery, and patients should be offered operation before this stage is reached.

In the correction of *congenital valvular stenosis* the valve itself is exposed by the measures previously mentioned The commissures are identified and carefully incised The configuration of the valve leaflets must be assayed The incision which separates the leaflets must be precise, and deviation from the line of cleavage may be associated with major degrees of insufficiency Such simple incision in the congenital type usually permits complete abolition of the gradient across the valve Frequently, even though there may be rudiments of three cusps, only two cusps are well developed Then the valve must be left as a bicuspid valve

Subvalvular obstruction is corrected by excision of the fibrous or muscular band, which is visualized by retracting the cusps of the aortic valve Since the mitral valve forms a part of the outflow tract of the left ventricle, it must be carefully visualized to prevent damage when the obstructing ring of subvalvular stenosis is removed

Risk of operation in such congenital lesions is extremely low, except in those patients who have been permitted to advance to a terminal stage of myocardial disease. The results of operation are good. Some cases are now being reported, however, in which patients have developed aortic insufficiency 1 year or more after operation. This apparently occurs in patients who have highly abnormal valvular tissue; the exact mechanism of the occurrence is not clear. Some congenital stenoses show a thickened, gelatinous-appearing valvular substance at operation. It seems that in some cases, the trauma of continued closure cannot be tolerated by these valves; it is likely that there is an intrinsic tissue defect which may require valvular replacement.

Patients with *acquired aortic stenosis* form a large group. By the time symptoms are manifest, these patients usually show evidence of severe valvular obstruction Calcification of the valve may be great; this is particularly evident in the pure stenotic lesions seen in patients over the age of 50. Calcification may be extensive, even in younger patients. However, a high grade of obstruction may also be present without calcification The criteria for selection of patients for operation are similar to those outlined for congenital lesions.

The operative correction of aortic stenosis or combined aortic stenosis and aortic insufficiency is now highly satisfactory. *It can be accomplished even in the presence of associated mitral valvular lesions.* The association of mitral stenosis and aortic stenosis is not unfavorable, and both valves can be repaired at a single operation The association of mitral insufficiency with aortic stenosis is also possible, but the risk of operation in this instance is higher than when the second lesion is mitral stenosis.

The operative procedure is individualized to meet the particular requirements of the pathologic alteration of the valve as seen at the time of operation After the stabilization of extracorporeal bypass and the induction of cardiac arrest, the aortic valve can be visualized by incision of the aortic root Calcium deposits can be removed from the valve in some instances; when this removal is combined with incision of the commissures, a satisfactory valvular function can be restored in selected cases With increasing experience, it has become more and more evident that replacement of all or part of the valve is necessary to achieve adequate opening of the valve in a high percentage of cases of aortic stenosis. During the past

possible form of surgical palliation for aortic *stenosis until, by open-heart methods, the* valve can be replaced. When one realizes the pathologic process with which the surgeon must cope and considers that pathophysiologic changes resulting from it are inexorable and follow a rather set pattern, it must become obvious that the only way to improve these results is by earlier selection of patients for surgery. Because, in recent years, most physicians have had considerably more experience with the problems of mitral stenosis than they have had with those of aortic stenosis, it would appear that much confusion exists as to what constitutes the proper indications for surgery in aortic stenosis. Patients are being referred for surgical relief of aortic stenosis using mitral stenosis indications. This practice must terminate for the two disease conditions present major differences The difference lies in the status of the left ventricular myocardium and the effects which these two valvular conditions exert upon the integrity of this structure The left ventricle is the *cornerstone of the heart.* Despite numerous and repeated bouts of pulmonary edema and right ventricular failure, the left ventricle in mitral stenosis has been spared and remains a strong and effective chamber. Actually, valvular obstruction at the mitral level has provided a measure of protection It follows then that decompensation in mitral stenosis is essentially right heart failure. With the establishment of more normal mitral valvular mechanics by surgery, the left ventricle can resume its fundamental role of maintaining total circulation effectively Thus, even if one waits in mitral stenosis for numerous bouts of congestive failure to occur, these patients may still be salvaged to a high degree because of the highly effective action of the left ventricular myocardium This pattern has pervaded the physician's thinking and has acted as a model for the reference of all patients with valvular disease for surgery The delay and wait for the signs and symptoms of decompensation are the greatest single factors accounting for the poorer results that are *often obtained in the surgery of aortic stenosis.*

It must be realized and repeatedly emphasized that, from the very beginnings of aortic stenosis, the brunt of the obstructive effect is absorbed by the left ventricle itself. It follows, therefore, that when the patient with aortic stenosis shows signs of decompensation his cardiac failure means left ventricular failure One cannot wait in aortic stenosis, therefore, until pulmonary congestion or frank congestive failure has developed, for myocardial reserve will then be all but gone. This distinct difference between the effect of mitral stenosis and aortic stenosis must be appreciated to the fullest before patients suffering from the latter condition will receive their best possible chance for survival and improvement. One has only to appreciate the fact that 17 of the 19 operative deaths in this series were in patients who had already experienced left ventricular failure to comprehend that new and realistic criteria must be established if these persons are to be given a *fighting chance.* Furthermore, once surgery has been performed, these patients must not be sent out into the world to fend for themselves (medically speaking). They need careful medical advice and management indefinitely. Even in those patients who have obtained the best hemodynamic response at the time of surgery, one must appreciate the fact that the left ventricle for years has been taxed to its uttermost and now needs intelligent careful support for its remaining lifetime To recapitulate then: when the nature of the pathologic condition in *aortic stenosis* is fully appreciated, when the physiologic and myocardial effects of this condition are recognized, when the patient is referred for surgery prior to left ventricular failure, and when surgery is performed by a swift and simple technique, then, and only then, will patients suffering from this most difficult of all valvular lesions be given their best chance for survival and maximal functional improvement

prosthesis has brought the correction of aortic stenosis and aortic insufficiency into a common ground. Recognition of the varied anatomic lesions that can produce aortic insufficiency has permitted direct, highly specific repairs based upon the pathologic lesion.

A list of the common causes of aortic regurgitation follows

1. Congenital
   a. Abnormality of valvular substance, including fenestration of one or more leaflets
   b Valvular insufficiency associated with a ventricular septal defect and prolapse of a leaflet
2 Traumatic
   a Penetrating
   b Nonpenetrating
3 Rheumatic
   a. Pure aortic insufficiency
   b Aortic regurgitation combined with stenosis
   c. Combined valvular disease
4 Syphilitic
   a Involving the aortic valve cusps
   b Involving the aortic valve annulus and base of the aorta
5 Endocarditic
   a Acute
   b Subacute
6 Caused by idiopathic dilatation of the aortic root
7 In Marfan's syndrome
   a With dissecting aneurysm
   b With dilatation of the ascending aorta
8. Caused by dissecting aneurysm
   a Acute
   b Chronic
9 Due to aneurysm of the sinus of Valsalva
   a Unruptured
   b With rupture into the right atrium, either ventricle, or either atrium

Each of these lesions may be associated with specific groupings of pathologic variations in the valve or the aortic root to produce aortic insufficiency. These variations, however, may all be considered as mechanical defects due to (1) loss of substance of one or more aortic cusps, (2) a disruption of one or more aortic cusps, (3) scarring and shortening of one or more aortic cusps, (4) prolapse of one or more aortic cusps, (5) separation of commissures, (6) communication between the aortic root and a cardiac chamber; (7) dilatation of the aortic annulus, or (8) loss of support of one or more aortic leaflets.

While localized lesions do occur, it has been interesting to note that generalized involvement tends to be the rule. This is particularly noticeable in those lesions associated with endocarditis in which there is thinning out of leaflets, which do not appear to have been seriously damaged by vegetations This process, however, is associated with a great decrease in the ability of the leaflet to withstand closing pressures. All those lesions which involve major disruption of aortic valvular substance—whether a shortening or lengthening of the leaflets, or detachment from its support—are corrected by replacement of the aortic valve with a prosthesis. Lesions associated with communication with one of the cardiac chambers may be corrected by closure of the communication and support of the suture line, usually with Teflon felt and Teflon cloth. In complicated lesions, it may be necessary to approach the lesion both from the ventricle and from the aorta simultaneously. All such procedures are done *under cardiac arrest*, in a manner similar to that used for aortic stenosis In a group of 175 patients in whom cardiac arrest had been induced with cold alone, there have been only two failures to resuscitate.

When the authors have used *aortic valve replacement* for the correction of aortic insufficiency, the over-all mortality rate has been 15 per cent for the last 50 patients. *Partial valve replacement* has been carried out in another 70 patients, with a slightly lower mortality rate These patients include many individuals who were far advanced in their disease, who were taken early in the series, and who probably would have survived with the methods now in use The authors have continued to accept patients who are far advanced in their disease, but in whom failure is controllable under very strict management in the hospital. In such patients, risk of operation is distinctly higher than the average, and these cases contribute in a large measure to the over-all mortality rate

Dissecting aneurysms form a specific category, in these patients, aortic valve replacement may not be required but *replacement of the ascending aorta* may be necessary to affect cure.

Dissecting aneurysms which arise in the ascending part of the arch may or may not be associated with aortic insufficiency. In patients with aortic insufficiency, correction of the dissection is essential, even though a spon-

procedure. The ability of the myocardium to resume a normal workload following the arrest is excellent. This has been true in extremely large hearts and in a far-advanced stage of the disease. *Perfusion of the coronary arteries* can also be utilized either at normal temperatures or under conditions of moderate hypothermia. This likewise maintains myocardial function at satisfactory levels.

The many processes that attack the aortic valve produce lesions of highly variable character. Some of them permit a reconstruction of the aortic valve components by measures which employ only the tissues of the valve itself. However, the majority of the situations do not fall into this category. There is usually such loss of substance, distortion, or loss of mobility that function cannot be fully restored by simple maneuvers. In such cases *a substitute for the aortic valve* must be available. In all operations upon the aortic valve, whether for repair of aortic stenosis, of aortic insufficiency, or of a combination of the two, the surgeon must be prepared to replace part or all of the valve. Such prostheses have been made of *Teflon* cloth or *Dacron* cloth impregnated with silicone rubber, as single leaflets and as total valves. The self-sealing, Dacron-silicone-impregnated valve has been widely used and has been highly satisfactory. These valves have been in place for more than 2 years and have continued to function satisfactorily. Partial and total valve replacements have been made in over 100 patients with restoration of normal hemodynamics.



Fig. 7-70. Severely calcified aortic valve that has been converted into a bicuspid structure because of the obliteration of one of the commissures. There are calcific deposits on the superior aspect of the leaflet, as well as on the inferior surface. It may be possible to mobilize the valvular structure to a functioning unit by adequate calcific debridement, however, in others, valvular replacement is the only satisfactory treatment.

It should be emphasized that patients with aortic valvular disease are usually seen relatively late in the course of the disease and tend to have a greater degree of left ventricular impairment than patients with other valvular lesions. For this reason, they require careful selection and meticulous pre- and postoperative management. A thorough understanding of the pathologic lesions and their variants is the basis of a satisfactory operative repair of aortic stenosis, aortic regurgitation, disease of the ascending aorta, and combined lesions.

AORTIC STENOSIS

Aortic stenosis may be broadly classified into congenital valvular, congenital subaortic, and acquired valvular types, and left ventricular outflow-tract hypertrophy. Of these, the *congenital valvular and subvalvular types* are the simplest pathologically and are usually easily recognized clinically. They may be associated with other congenital lesions, particularly coarctation. The valvular type is frequently presented as a *bicuspid valve* or with some other distortion of the normal architecture of the valve (Fig. 7-70). Severe obstruction frequently gives rise to symptoms in childhood, but lesser degrees may not manifest themselves until later in life. Left heart catheterization with simultaneous left ventricular and aortic root pressures, calculation of orifice size, and aortography or angiocardiography are helpful in delineating the lesions. Left ventricular angiography is particularly helpful in the separation of ventricular outflow-tract hypertrophy from other types of aortic stenosis in the young adult. Gradients alone are not necessarily reliable evidence of degrees of obstruction, they must be considered in relation to the cardiac output and other studies in the individual case. In the congenital lesions, evidence of a high degree of obstruction is an indication for operation. Patients who manifest symptoms, especially those who evidence progression by increasing symptoms or signs, are advised to have operation. At the present time, patients with *left ventricular outflow-tract hy-*



Fig. 7-71. Aortic cusp prosthesis, made of Dacron cloth and impregnated with silicone rubber, sutured into position at the aortic annulus. The unit can be used singly, or two or three similar cusps may be used to reconstruct the valve. The reflex edge seen through the leaflet is not silicone-covered; this allows the ingrowth of tissue from the aortic wall to penetrate this portion of the cusp alone.

year, it has been the authors' policy to perform *partial or total aortic valve replacement* in all but a few highly selected cases Excision of one or two leaflets of the aortic valve is frequently adequate, particularly when one can remove essentially all the calcium from the remaining cusp or cusps, so that there is excellent mobility. The valve cusp replacement used by the authors for these repairs has been the silicone-impregnated Dacron-cloth cusp with the reflex edge to provide the self-sealing feature (Fig. 7-71). This provides immediate competence and enables one to correct any major or minor degree of aortic insufficiency. The valve is totally replaced in an increasing percentage of cases (Figs. 7-72 and 7-73)

The mortality rate for operations for pure aortic stenosis has been constantly decreasing, at present, it approximates 10 per cent in patients who are not in intractable congestive heart failure prior to operation The authors currently believe that patients in the terminal phase of their disease and expected to die within a matter of weeks are not candidates for operation, as they have already manifested an inadequate left ventricular musculature.

AORTIC INSUFFICIENCY

The treatment of aortic insufficiency has shown similar improvements in both the technical aspects of correction and the pre- and postoperative management of the patient. Experience during the past 2 years has shown that *total aortic valve replacement* for the treatment of aortic insufficiency has been an effective and increasingly safe method for the treatment of this serious problem. The development of a satisfactory subcoronary valvular



Fig. 7-72. Three 1¼-in. leaflets in position prior to their advancement into the aortic root. The destroyed cusps had to be completely replaced to restore normal hemodynamics. This view also clearly outlines the necessity of an uncluttered field in this procedure and demonstrates one of the advantages of cold arrest in carrying out this operation.



Fig. 7-73. The three leaflets sutured into the normal anatomic position of the aortic valve. In the collapsed aorta the individual leaflets appear compressed, but with refilling of the aortic root with blood, these leaflets coapt perfectly during ventricular diastole. Restoration of normal blood pressure was immediate following resumption of a normal cardiac beat.

[illegible] sociated with episodic or constant peripheral edema and ascites (or the latter alone), usually never having suffered the usual pulmonary symptoms secondary to pulmonary hypertension Such patients are not ordinarily dyspneic or orthopneic.

Venous Pulsations. When seen to be abnormally vigorous in the neck, these pulsations suggest tricuspid disease, regardless of whether they are caused by regurgitation or by atrial displacement of an otherwise flexible stenotic tricuspid valve "diaphragm" [2] The "liver pulsations" repeatedly referred to are possibly transmitted cardiac impulses applied to the surface of the liver itself [3]

Cyanosis. With or without jaundice, cyanosis would indicate either peripheral stasis or pulmonary stasis and could be a manifestation of mitral stenosis alone

Right Atrial Enlargement. This finding is present in Lutembacher's syndrome and tricuspid insufficiency, as well as in tricuspid stenosis Enlargement may not be present if the wall of the atrium is "protected" by mural thrombosis or myofibrosis

Diminished Pulmonary Arterial Dimensions as Seen Radiologically. This change is typical and most marked if the tricuspid stenosis matured before the mitral stenosis

Localized Diastolic Murmur at the Lower End of the Sternum. There is usually great difficulty in interpreting the significance of the diastolic murmur, and rarely is a diagnosis of dynamic tricuspid stenosis made on such auscultatory findings. A clear-cut demonstration, however, is helpful [4]

[2] The last mechanism is unlikely. Vigorous atrial contraction may cause *presystolic* pulsations in the neck veins and the liver No systolic pulsation of significant size occurs without tricuspid regurgitation, relative or absolute (functional or organic). *Editor*

[3] Graphic tracings recorded at the epigastrium and over the liver easily permit one to differentiate a transmitted cardiac thrust from an expansive liver pulsation (*See* Chap 11, Part 3, Chap 7, and Part 1, Chap. 10) *Editor*

[4] Inspiratory accentuation of this murmur, as well as of an *opening snap*, is evidence of the tricuspid origin of the sound vibrations, in contrast with the mitral origin (sign of Rivero Carvallo). *Editor.*

Hemodynamic Abnormalities. With pressure tracings taken from the right atrium, it was assumed originally that the presence of a large A wave occurring during atrial contraction would indicate stenosis of the tricuspid valve. However, this observation appeared to lack the necessary refinements.

More recent investigators have pointed out that the *mean* diastolic gradient across the valve offers the best aid in laboratory diagnosis. Killip and Lukas have observed that: "An elevated *mean* gradient, widening with exercise, was considered *the* most reliable physiologic criterion for the diagnosis of tricuspid stenosis."

TREATMENT

Since there is no medical relief for this mechanical obstruction, operative intervention is essential in the patients with clinical symptoms. Operative mortality and morbidity are and should be very low. The procedure is simply a matter of incising one of the fused commissures with a knife to a degree that will allow free flow of blood through the tricuspid orifice while preserving its competence. The question of simultaneous mitral and tricuspid commissurotomies as opposed to staged sequential operations can be solved on the basis of individualized judgment in each case rather than on inflexible surgical preference.

COMMENTS

Appreciating the widespread use of commissurotomy in the treatment of mitral stenosis, we are faced with the question of how many cases have had unrecognized tricuspid stenosis of a degree serious enough to obviate a clinical cure. In view of a certain percentage of failures in otherwise adequately operated patients, attention might be directed with profit toward the possible coexistence of tricuspid stenosis. In such instances, cardiac catheterization usually will be decisive.

It was previously reported that the mitral valve is involved in 90 per cent of individuals dying as a result of chronic rheumatic valve disease, while the tricuspid valve is involved in 30 per cent. The mitral valve *only* is involved in 23 per cent, while there is no instance of involvement of the tricuspid valve *only* The incidence of coexistent involvement

taneous re-entry may occur distally into the aorta.

Aortic insufficiency caused by dissection arising in the ascending aorta may be produced by detachment of an aortic leaflet in the zone of the commissure from its normal support by the dissection or by extreme dilatation of the aortic annulus. *Resection* of the area of dissection and *replacement by graft* after closure of the distal double lumen eliminate the diseased aortic segment The valvular insufficiency may be corrected by resuspension of the aortic valve leaflet and closure of the proximal dissection. Under some conditions, it is possible to resuture the area of the dissection after resection of a short portion of the ascending aorta. By converting both the proximal and distal double-lumened aorta into a single lumen, direct resuture may be achieved in some cases The authors have now operated on seven patients with such dissections and associated aortic insufficiency, with five survivors.

Surgical correction of lesions of the aortic valve and the aortic root has made great progress. Essentially all the pathologic problems of this area are now susceptible to a solution. It can be anticipated that excellent restoration of valvular function can be achieved in aortic stenosis, aortic insufficiency, and combined lesions, regardless of the origin of the lesion. Careful selection of the patients for surgical correction, preoperative evaluation, and meticulous postoperative management are essential to success.

dominal pains It was thought that she had suffered an embolism to the abdominal viscera, and she was treated conservatively. On Oct 17, 1955, paracentesis was done, with the removal of a considerable amount of amber-colored fluid The patient became asymptomatic and was discharged on Oct. 20, 1955 It was thought at the time of operation that, because of the severe deformity and heavy calcification of the mitral valve, a less than desirable opening of the mitral valve had been accomplished

The patient's condition remained fairly good, requiring occasional paracentesis to control the ascitic fluid. She was readmitted on May 24, 1956, for further study. Forty-eight hours later, the patient developed cyanosis of the left leg, and it appeared that she had an embolism to the left femoral artery She was treated with caudal anesthesia over a period of several days and improved. It also became apparent, on the basis of the history together with the x-ray findings, that the patient had tricuspid stenosis. Subsequently, she was operated upon on June 13, 1956, at which time the tricuspid valve orifice was found to measure 8 by 2 mm, with a slight element of regurgitation Using guillotine knives, two commissures were opened without difficulty, resulting in an orifice measuring 25 by 30 mm and no increase in the minimal regurgitant element The patient responded well, began to lose weight without difficulty, and was discharged on July 18, 1956

She was readmitted on Sept. 13, 1956, because of recurrent ascites and 4+ edema of the ankles. Over a period of 3 days, 14,700 ml of ascitic fluid was removed, the patient responded well and was discharged on Sept. 19, 1956.

She was readmitted on Oct. 27, 1956, again with severe anasarca plus cyanosis around the lips. Paracentesis was done, resulting in a 30-lb weight loss, together with symptomatic improvement. On Nov. 10, 1956, she was placed on Diamox, during the following week, it was felt that she developed a low-salt syndrome and was treated accordingly. On November 19, the beneficial results of this treatment were seen in that the patient, who had been lethargic and disoriented, now became mentally clear and the ascites was greatly reduced On Nov 20, 1956, the patient suddenly ceased to breath, and, because of this sudden occurrence, it was felt that she had suffered a pulmonary embolism

These two cases occurred in a series of 400 cases which were operated on for mitral stenosis and would suggest an incidence of 5 per cent, which is in line with the previous deductions It is interesting to note that the symptomatic effects of the tricuspid lesion were not clearly present at the time of the mitral valve surgery and in both cases appeared to be accentuated after the mitral surgery

1

Surgery of tricuspid stenosis

THOMAS J. O'NEILL

Tricuspid valvular disease in adults is usually rheumatic in origin. As seen in the mitral and aortic valves, severe anatomic distortion of the leaflets of the tricuspid valve produces insufficiency, stenosis, or an element of each Such deformities, when slight, cause no physiological derangements but, when marked, interfere noticeably with cardiovascular function From a clinical standpoint, the terms *adynamic* and *dynamic* tricuspid disease seem applicable.

Whereas insufficiency of the tricuspid valve may be *primary,* when due to distorted valve leaflets, or *secondary,* when due to changes incident to severe right heart failure, *stenosis is always an organic involvement.* The size of the orifice is of considerable importance in that there probably exists a critical area above which insufficiency predominates and under which stenosis predominates This area has not as yet been closely defined and requires further observation.

Rarely does this disease exist as a solitary valvular defect Reports of autopsy studies demonstrate that its highest incidence is in association with both aortic and mitral disease and its next highest incidence is in association with mitral valve involvement. A decisive clinical diagnosis usually cannot be made because of the masking effects of the mitral valve lesion. Therefore, the successful surgical treatment for stenotic valvular disease now imposes a greater demand for more accurate methods of diagnosis of stenosis of the tricuspid valve, since this lesion may no longer be regarded as having merely prognostic importance.

Operative attempts have been made simultaneously on the combination of aortic and mitral stenosis with some success, but it is apparent that both of these valves, located as they are in the left heart, render operative appraisal less difficult and intervention more feasible than in the case of the tricuspid valve. The tricuspid valve, being on the opposite side, requires a more formidable approach for simultaneous surgery or else necessitates a two-stage operation.

DIAGNOSIS

The diagnosis of tricuspid stenosis is not easy to make, mainly because of the absence of unambiguous cardinal features This problem is the greater because the principal signs and symptoms are obscured by similar findings often seen in solitary mitral stenosis.[1] During life, there are only two methods of differentiation available. (1) elimination of the symptoms secondary to mitral stenosis by means of a mitral commissurotomy, thereby allowing a residue of provocative symptoms that suggests a dynamic tricuspid stenosis, (2) hemodynamic studies obtained through *right heart catheterization* which, indicating a significant *diastolic gradient across the tricuspid valve,* would support the diagnosis of predominant stenosis

The most important symptoms and signs suggestive of tricuspid stenosis may be listed as follows·

[1] The predominance of ascitis, severe congestion of the venous system, and a large and firm liver while orthopnea is absent and the patient is able to walk for a long period of time are typical of tricuspid stenosis. *Editor.*

of psychotic involvements would be much lower than evaluations by psychiatrists is not surprising, as such estimates are often made *in retrospect*, that is, by reviewing charts of discharged patients. If, at the time that the patient was treated, the staff was not aware of the need for such information, much of the communication regarding the patient's emotional state at the time of operative hospitalization may be conducted orally, without explicit notes in the patient's record regarding his moods, feelings, or confusional behavior It seems, therefore, reasonable to assume that the estimated 3.14 per cent psychoses reported by Bolton and Bailey represent a crude minimum estimate and that the other relatively small samples reported by psychiatric research studies represent estimates of psychologic involvements based on more detailed and systematic observations

Our rough estimate made from these psychiatric reports of psychotic *symptoms*, or "obvious emotional disturbances," during the immediate post commissurotomy period was for the study of Bliss et al, 16 per cent, Fox et al, 19 per cent, and Kaplan, 17 per cent—indicating an impressive uniformity of findings In addition, all three studies stress the fact that a large number of other commissurotomy patients had considerable psychologic difficulties of various kinds It appears, therefore, likely that we are faced with a more general type of psychologic reaction than meets the eye at first sight

Fox et al and Kaplan discuss the psychiatric aspects of the phenomenon However, neither of these studies has systematically utilized psychologic tests Therefore, though providing a qualitative analysis of the personality dynamics and psychologic conflicts, they fail to quantify the psychologic functions involved in the observed depressions, suicide attempts, and psychotic confusional states—any of which can be caused by a disruption of a variety of underlying psychologic factors Further, the studies reviewed above have not utilized control groups and, therefore, fail to establish the specificity or generality of the observed psychiatric disturbances

1 Are these psychologic manifestations related to the presence of heart disease in general or to mitral stenosis in particular?

2 Is the impact of any surgical trauma upon the cardiac organ a sufficient immediate precipitating factor to produce the disruption of psychologic functioning, or is the particular type of surgical technique of mitral commissurotomy more closely related to the triggering off of psychologic dysfunctions?

3. To what extent is the etiology of mitral stenosis, which is assumed to be a repercussion of rheumatic fever in its various forms, involved as a causal factor?

4. Are the psychologic disturbances of a functional nature, or are they related to neurologic involvements of the central nervous system?

5 To what extent are the psychologic changes, when they occur, permanent, and to what extent are they reversible?

Our study attempts to throw some light on these unanswered questions.

METHOD

The psychologic examinations were part of an interdisciplinary study, which included a thorough *test battery* administered at the time that a complete medical study of the heart condition of the patient was made. Concomitantly, neurologic and psychiatric examinations were given each patient.

Comparable groups of individuals with rheumatic heart disease and with other heart diseases were included. To date 75 patients have been studied Of these patients, 57 had rheumatic heart disease. The rheumatic heart disease group consisted mostly of patients with mitral stenosis alone or in combination with other cardiac involvements Various degrees of aortic valve dysfunction were noted in 9 of these patients Mitral commissurotomy was performed in 33 patients, and 2 of the rheumatic heart disease group had Hufnagel valves inserted

Two patients with mitral stenosis failed to survive commissurotomy, and one died 10 days after surgery.

The ratio of females to males in the rheumatic group was approximately 2:1.

Cardiac involvements of various kinds not attributed to rheumatic fever were present in 18. Of these patients, 13 had congenital defects and 5 had coronary artery disease. The characteristics of this group are given in Table 7-13.

No attempt at selection was made on the basis of age, duration of cardiac illness, severity of symptoms, occupation, or the attending physician's impression of the emotional state of the patient. All patients were white, North American born individuals, and had attended American schools All operations were performed by the

of the mitral and tricuspid valves, excluding aortic and pulmonic lesions, is 7 per cent.

Cooke and White report a total of 66 cases: 59 cases of solitary mitral valve involvement and, in addition, 7 cases having combined mitral and tricuspid involvement. Of these, there were four instances of mitral stenosis combined exclusively with tricuspid stenosis, indicating that mitral valve disease, exclusive of aortic and pulmonic valve disease, is complicated by tricuspid stenosis in 6 per cent of the instances.

Unfortunately, available series are not detailed enough to allow appraisal of these relationships, and it is still hoped that future reports will better illuminate this problem.

PERSONAL EXPERIENCE

Two patients with tricuspid stenosis underwent surgical treatment for this valvular deformity at a time subsequent to mitral commissurotomy.

Case 1 A 36-year-old white woman was first referred on Oct. 10, 1949 She had a history of chorea at the age of 7 years At the ages of 19 and 22 years, joint pains and fever were present She then became bedfast with continual cardiac decompensation during the next 8 years. She recovered somewhat, but at the age of 33 experienced a 2-day episode of coma For the following 8 years, she was treated with digitalis, mercurial diuretics, and a low sodium diet.

On admission, the blood pressure was 140/84 Normal sinus rhythm was present An apical diastolic murmur, a sharp mitral 1st sound, and an accentuated pulmonic 2d sound were heard. *Fluoroscopically, the right ventricle and pulmonary artery were enlarged* The atria and left ventricle were not enlarged. The ECG showed right axis deviation *Cardiac catheterization showed an average systolic pressure in the right atrium of 5 mm Hg while the diastolic pressure was zero* The systolic pressures averaged 16 mm Hg in the right ventricle while diastolic pressures were zero.

Mitral commissurotomy was performed on Oct 14, 1949. The mitral slit was 20 mm in length and was enlarged to 35 to 45 mm, with resulting good valve function The patient was discharged after 12 days and returned in 3 months for checkup. She was improved but had had ankle edema on one occasion There was no evidence of right or left heart failure.

One year following the mitral operation, the patient developed edema of the face and breasts and experienced exertional dyspnea. There was also ankle edema but no hepatomegaly or cyanosis. Systolic pulsations were noted in the neck veins. The lungs were clear. The 2d pulmonic sound was accentuated, but the mitral 1st sound was not. There was a *rumbling diastolic murmur, heard between the mitral area and the xyphoid.* The ECG showed P wave abnormality and right axis deviation Cardiac catheterization now showed *systolic pressure in the right atrium of 12 mm Hg on the average, as compared to 25 mm Hg in the right ventricle. The average diastolic pressure was zero in the right atrium and −10 in the right ventricle.*[5]

A *tight tricuspid stenosis* was found at surgery on July 17, 1953, and this was opened adequately with a guillotine knife, enlarging a 13- by 2-mm orifice to one measuring 30 by 10 mm. In less than 1 hr postoperatively, all edema subsided. The patient was discharged in 10 days without evidence of right or left heart failure.

She has remained free of symptoms for the past 5 years

Case 2. A white woman was admitted at the age of 35 for the first time on June 19, 1955, complaining of "fluid in the stomach." She had been well until 3 or 4 months prior to admission when she began to notice that her abdomen was swelling. This became constantly worse. Paracentesis was done, and the laboratory report suggested the possibility of malignant cells She had no other serious symptoms. On examination, she was well developed and well nourished, in no distress. There was a grade III late diastolic murmur at the apex and some cardiac enlargement. The abdomen was soft; the liver edge was palpated two to three fingerbreadths below the costal margin and was nontender. There was some ankle edema.

Exploratory laparotomy was done of June 24, 1955, and 2 to 3 qt of cloudy ascitic fluid were withdrawn The liver was markedly enlarged and firm There was no nodularity present. A biopsy was done, which proved chronic passive congestion. The ascitic fluid showed no evidence of malignancy and there was no gross evidence of malignancy. The patient was readmitted on Sept. 21, 1955, and a mitral commissurotomy was done on Sept. 24, 1955. The patient responded well until Oct 12, 1955, when she experienced severe ab-

[5] These data should be interpreted as evidence of a definite tricuspid regurgitation, together with a tricuspid stenosis. The latter is revealed by a gradient of 10 mm across the tricuspid valve. (It is likely that the zero line was placed too low and the actual diastolic pressures were +10 in the atrium and zero in the ventricle.) As the previous catheterization had not revealed such a gradient, one could speculate that tricuspid stenosis had occurred in the 1-year interval between the first and second observation *Editor*

TABLE 7-14. BACKGROUND VARIABLES OF RHEUMATIC AND NONRHEUMATIC OPERATIVE AND NONOPERATIVE HEART PATIENT GROUP

Variable	*Rheumatic heart disease*		*Nonrheumatic heart disease*		*Totals* *
	Commissurotomy	*Nonop*	*Surgical*	*Nonop*	
No of cases	33	22	13	5	73
Sex.					
Men	10	6	5	2	23
Women	23	16	8	3	50
Age:					
Mean	39 6	41.6	37 0	42 0	39.9
Range	26–51	23–63	22–60	22–66	22–66
Years school					
Mean	11 1	12 0	10.7	11.4	11 3
Range	8–20	7–20	4–16	10–12	4–20
Religion					
Catholic	17	9	6	2	34
Protestant	16	11	7	3	37
Jewish	0	2	0	0	2
Marital status,					
Married	25	18	10	3	56
Divorced/sep	2	0	1	0	3
Never married	4	2	2	2	10
Widowed	2	2	0	0	4
No of children					
Mean	1 6	1 8	1 6	3 7	1.8
Range	0–6	0–8	0–3	1–8	0–8

* No averages are given for the rheumatic aortic surgical cases (Hufnagel) because there were only two patients in that group.

sler scale were used in test one, retest one, and retest three, Form I was administered, in retests two and four, Form II was used

DISCUSSION OF RESULTS

Table 7-15 shows the actual weighted scores on the eight subscales of the Wechsler-Bellevue used in this study, as well as the verbal, prorated performance, and full-scale I Q's for the combined group of rheumatic heart disease patients, as compared with the combined nonrheumatic heart disease patient group. Each group consists of nonoperative patients and operative patients in the preoperative stage

It is apparent that both groups are somewhat above average in their intellectual abilities It is characteristic of both groups, that is, of heart patients in general, independently of the etiology of the disease, that Digit Span is considerably lower than the rest of the Wechsler-Bellevue subscales Digit Symbols and Arithmetic tend to be somewhat impaired, but this does not occur with either the frequency or consistency of the impairment apparent in Digit Span As can be seen from Table 7-15 *none of the group mean differences reach statistical significance*, that is, the two groups do not differ from each other in any of the intelligence measures employed beyond the extent expected to occur due to chance

The lowered Digit Span reflects an impairment in immediate memory, which is often due to impaired attention A decrease in Arithmetic is often interpreted as impairment in the ability to concentrate on the task at hand Both of these scales are known to suffer under conditions of anxiety. The somewhat lowered Digit Symbols score may be due to the same reason.

I

Disturbances in psychologic functions and neuropsychiatric complications in heart surgery

MISHA S. ZAKS

Considerable psychiatric complications following mitral commissurotomy have been reported by several investigators.

Bolton and Bailey (1956) report two suicides and 3.14 per cent of psychotic episodes in the postcommissurotomy period in a statistical survey of 1,500 heart surgery cases. Bliss et al. (1955) analyzed hospital records of 37 patients who had undergone mitral surgery and found 4 cases of post-commissurotomy schizophrenic reactions, 2 of whom were transferred to the psychiatric unit. One of these 4 cases was known to have been psychotic also before surgery, and the operation caused a recrudescence of his schizophrenic process. In some of these patients, *delusions* were prominent, while in others *hallucinations* were reported. In addition, 2 of the 37 patients developed organic confusional states, "and 6 further patients, although not psychotic, were sufficiently anxious and depressed to merit comments by both physicians and nurses." This equals roughly 16 per cent of psychotic confusional states and an additional 16 per cent of less severe psychological disturbances.

Fox et al. (1954) studied 32 patients who had mitral surgery. In their report, 6 patients appear to have had "obvious emotional disturbances." This constitutes about 19 per cent of their sample, besides, several cases with less severe psychologic disturbances are discussed by these authors.

Kaplan (1956) studied 18 patients, who experienced mitral commissurotomy, for varying periods of time following surgery. He writes: "Many of the patients experienced emotional disturbances. One patient became psychotic and had to be transferred to the psychiatric ward. Two others described transient mild psychotic symptoms." One of these patients is also reported to have expressed suicidal thoughts and to have made an attempt to jump out of a window. In addition, Kaplan gives several examples of patients who manifested psychologic symptoms of various kinds, including a number of psychosomatic disorders. But, even disregarding all except the 3 cases who developed psychotic symptoms following commissurotomy, his study gives a frequency of 17 per cent of serious emotional disturbances.

The study reported here was begun in 1954 before any of the reports cited above had appeared. It was initiated in order to learn the causes of the unexpected psychological complications observed in postcommissurotomy patients at the Wesley Memorial Hospital. In the early experience of this hospital with mitral surgery, 2 patients had to be transferred to the psychiatric ward following mitral commissurotomy because of psychotic breaks, and two other patients committed suicide during the post commissurotomy recovery period.

PROBLEM

The above clinical observations indicate that serious psychologic disturbances in postcommissurotomy patients occur with considerably frequency. That a surgeon's estimate

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No. of cases	33	22	13	5	73
Sex:					
Men	10	6	5	2	23
Women	23	16	8	3	50
Age:					
Mean	39.6	41.6	37.0	42.0	39.9
Range	26–51	23–63	22–60	22–60	22–66
Years school:					
Mean	11.1	12.0	10.7	11.4	11.3
Range	8–20	7–20	4–16	10–12	4–20
Religion					
Catholic	17	9	6	2	34
Protestant	16	11	7	3	37
Jewish	0	2	0	0	2
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Widowed	2	2	0	0	4
No. of children					
Mean	1.6	1.8	1.6	3.7	1.8
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The lowered Digit Span reflects an impairment in immediate memory, which is often due to impaired attention. A decrease in Arithmetic is often interpreted as impairment in the ability to concentrate on the task at hand. Both of these scales are known to suffer under conditions of anxiety. The somewhat lowered Digit Symbols score may be due to the same reason.

TABLE 7-13. DISTRIBUTION OF VARIOUS CARDIAC DEFECTS IN THE NONRHEUMATIC HEART DISEASE GROUP

Type of defect	*Frequency*	*Sex*		*Operated*	*Deaths*	
		M	*F*		*No*	*Time*
Interatrial septal defect	6	0	6	5	1	At surgery
					1	One year postop
Pulmonary stenosis	4	1	3	2		
Patent ductus	2	0	2	2	1	At surgery
Marfan syndrome	1	1	0	1	1	Two days postop
Coronary disease	5	5	0	3	1	Half-year postop
					Immediate	Delayed
Total	18	7	11	13	3	2

same surgical team. The pre- and postoperative treatment was similar for all patients who underwent heart surgery, as they were attended to by the same staff, were treated on the same wards, and were assigned either to single or two-bed private rooms, whenever such were available.

Table 7-14 summarizes the relevant background data for the various groups, as well as for the entire study.

The following psychologic tests were administered to the patients. Wechsler-Bellevue Intelligence Scale (eight subscales), an organic battery for generalized deterioration and cortical involvement (Yacorzynski), the Rorschach, the Draw-a-Person test, the Thematic Apperception Test, the Bender-Gestalt, Gottschaldt Figures, the Street Gestalt Completion test, and a personality inventory.

The patients were tested before and approximately 3 weeks after the heart operation At that time they were also reexamined by the neurologist and the psychiatrist. Following this, they were retested after 6 months and at yearly intervals thereafter Up to the present time, the maximum number of retests has been five.

In the analysis of the data carried out to date, the commissurotomy group has been compared with the group of nonrheumatic heart surgery cases, preoperatively and at the stated postoperative intervals, to determine which psychologic differences can be ascribed to commissurotomy, as opposed to other types of heart surgery The surgical groups were also compared with their respective nonoperative control groups in order to determine what psychologic changes, if any, are characteristic of the immediate preoperative condition of the patients. Further, all rheumatic heart disease patients, that is, those who eventually underwent commissurotomy as well as those who did not, were pooled to draw a statistic comparison with all the nonrheumatic heart disease patients before attempted surgical intervention. This was done to determine if rheumatic heart disease in general is psychologically distinguishable from nonrheumatic cardiac involvements

This chapter will deal with the results obtained from the objective psychometric tests only. this includes the Wechsler-Bellevue Intelligence Scale, the Yacorzynski battery for organic brain involvement, the Gottschaldt Figures, and the Street Gestalt Completion test.

The results obtained from the application of the Wechsler-Bellevue Intelligence Scale will be presented first. This test samples a wide variety of performance, reflecting intellectual ability. As it includes a large number of various skills, some of which require mainly verbal abilities, while others are concerned mostly with visual-manual performance, the Wechsler scale provides separate estimates of verbal and nonverbal intelligence, each based on several tasks. It also provides a full-scale I Q based on all subtests The test also has the advantage that the individual subscales can be independently analyzed to provide information about the specific functions they are designed to measure within the general realm of mental abilities The various subscales have been normalized so that approximately equal scores on each subscale are expected from the testee. Significant discrepancies between the weighted scores provide an indication of deficit in specific abilities, some of which are more prevalent in certain functional psychiatric disorders, while others are more frequent in cases of organic brain deficit and in mental deterioration due to advanced age.

In this study, two alternate forms of the Wech-

Design. This deficit persists in the postcommissurotomy group throughout the four postoperative retests, representing a period of more than 3 years. The Digit Symbols subscale also shows a significant deficit, however, recovery is evident at the third postoperative retest, one year after surgery. Comprehension is significantly impaired only during the first postoperative retest, but not during the subsequent periods. Consequently, this is an impairment of very short duration

The impairment in performance I.Q. and full-scale I.Q. in the first postoperative retest reflects the initially widespread disturbance in intellectual functioning immediately following commissurotomy It is apparent that, in the subsequent retests, the deficit is mainly *in some specific areas* of intellectual functioning, although it is not confined to a single subscale, as Similarities and Picture Completion also show a tendency toward impairment in postcommissurotomy patients

The characteristic failure of the commissurotomy group to reach the functioning level of the nonrheumatic surgery group in the performance on the Block Design test throughout the 3-year follow-ups indicates that the impairment is most pronounced when the patients are confronted with a visual-manual motor task which requires nonverbal abstract reasoning ability It is often characteristic of patients who sustain some injury to the central nervous system that Block Design shows a significant impairment

In order to evaluate the scope of the impairment in psychologic functioning observed on the Wechsler-Bellevue, the results obtained from the perceptual and concept formation tests included in this study will be analyzed These tests were chosen in order to investigate possible impairments related to organic brain involvements

The Yacorzynski battery for organic brain involvement consists of a Concept Formation test for generalized deterioration and three perceptual tests for cortical involvement The battery has been described by Yacorzynski and Davis (1945)

The Concept Formation test is of the block-sorting type, in some respects similar to the Vigotsky and Weigl block-sorting materials The test consists of 16 blocks which can be sorted in 8 different ways, according to form, color, area, height, and volume of the blocks and form, color, and area of the designs on top of the blocks. Yacorzynski states that this test measures generalized deterioration in organic brain functioning. Cross-validational evidence for this test has been published by Rosenberg and Altrocchi (1958). Theoretical evidence that concept formation, as indicated in object-sorting tasks, is related to organic brain functioning has been provided by Goldstein and Sheerer (1941) and others.

That difficulties in the perception of visual illusions, fluctuating figures, and ambiguous designs are characteristic of individuals with cerebral damage has been reported repeatedly by many investigators in the field of organic brain syndrome testing.

The Gottschaldt Figures and similar hidden-figures tasks have been used for purposes of detection of brain damage by a number of investigators, particularly Gelb and Goldstein (1920), Teuber et al. (1951), and Battersby (1953). H. L. Teuber, who used this test extensively, states that impairment on hidden-figure tasks follows lesions in any lobe of the brain:

> Injuries of higher visual pathways resulting in permanent field defects were not a necessary condition for difficulties with hidden figures The impairment exists with and without concomitant symptoms in the same sense modality through which the task is perceived. In fact, we need not assume that the impairment is limited to vision. . . . However, impairment was significantly related to the presence of aphasia, since aphasics as a group did considerably worse than nonaphasic brain-injured subjects, who were surpassed, in turn, by the controls

The Street Gestalt Completion test provides a measure of meaningful closure, a perceptual function which is assumed to be of basic importance in perceptual organization.

It is evident from Table 7-17 that Standard Illusions, Gottschaldt Figures, and the Gestalt Completion test show *statistically significant differences between the total (the non- and preoperative) rheumatic cardiac group and the nonrheumatic cardiac patients*. In order to evaluate to what extent the observed perceptual impairments are due to the presence of rheumatic heart disease, or to what extent they are specifically related to the immediate preoperative state of the mitral stenosis group, the precommissurotomy patients were compared with the nonoperative rheumatic pa-

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					1	One year postop
Pulmonary stenosis	4	1	3	2		
Patent ductus	2	0	2	2	1	At surgery
Marfan syndrome	1	1	0	1	1	Two days postop.
Coronary disease	5	5	0	3	1	Half-year postop.
Total	18	7	11	13	Immediate 3	Delayed 2

same surgical team The pre- and postoperative treatment was similar for all patients who underwent heart surgery, as they were attended to by the same staff, were treated on the same wards, and were assigned either to single or two-bed private rooms, whenever such were available.

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In the analysis of the data carried out to date, the commissurotomy group has been compared with the group of nonrheumatic heart surgery cases, preoperatively and at the stated postoperative intervals, to determine which psychologic differences can be ascribed to commissurotomy, as opposed to other types of heart surgery The surgical groups were also compared with their respective nonoperative control groups in order to determine what psychologic changes, if any, are characteristic of the immediate preoperative condition of the patients. Further, all rheumatic heart disease patients, that is, those who eventually underwent commissurotomy as well as those who did not, were pooled to draw a statistic comparison with all the nonrheumatic heart disease patients before attempted surgical intervention. This was done to determine if rheumatic heart disease in general is psychologically distinguishable from nonrheumatic cardiac involvements.

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posed to measure, the possibility has to be considered that some interference with normal cortical functioning is already present in this group before mitral surgery is performed. This impairment, such as it is, evidently does not influence either intellectual functioning or conceptual reasoning, as measured by the Wechsler-Bellevue and the Concept Formation test.

The immediate postoperative retest indicates a persistence of the preoperative impairment on the Yacorzynski cortical tests, the Gottschaldt Figures, and the Gestalt Completion test in the mitral commissurotomy group. In addition, however, the Concept Formation test for generalized deterioration, not previously impaired, now reaches a significant impairment level (at a 0.02 level of significance).

Possibly, following commissurotomy there is a spread of dysfunction in the perceptual-motor spheres, producing an impression of generalized deterioration in performance ability. This complements the results previously obtained in the Wechsler-Bellevue analysis, where the immediate postcommissurotomy scores suggested a similar effect of generalized impairment in the sphere of intellectual abilities.

Table 7-19 presents, however, a somewhat shifting picture. There is a tendency toward recovery on the Illusions after the first retest, and some tendency toward recovery also seems indicated on the Gottschaldt Figures. However, the Gottschaldt Figures seem to remain somewhat impaired, as the t test differences still remain at a 0.10 level of statistical significance at the subsequent retests. The fact that the Fluctuating Figures test reaches statistical significance at the second postoperative year for the first time seems surprising. However, in view of the very large dispersion of raw scores in both the Ambiguous Figures and the Fluctuating Figures, these measures can be expected to give somewhat erratic results.

While this study suggests that certain intellectual and perceptual functions show various degrees of impairment in the commissurotomy patient group, it should be considered that these changes are subtle and become apparent mainly in a comparison of these patients' test results with those of other patient groups. They are, to an extent, due to the failure of the commissurotomy group to improve scores in repeated test sessions, rather than due to dramatic losses in performance ability upon retesting.

While there is considerably less learning evident in the commissurotomy group than in the nonrheumatic heart surgery group in repeated testing, some learning, nevertheless, does occur, as the scores of the commissurotomy patient group do show some increase in subsequent trials.

It deserves mention that clinical psycholo-

TABLE 7-19 ORGANIC AND PERCEPTUAL MEASURES SIGNIFICANCE OF GROUP MEAN DIFFERENCES BETWEEN COMMISSUROTOMY PATIENTS AND NONRHEUMATIC HEART SURGERY PATIENTS POSTOPERATIVE RETESTS 1, 2, AND 3

Test	*Postop 1*		*Postop 2*		*Postop 3*	
	df	*t*	*df*	*t*	*df*	*t*
Concept Formation	37	2.32 *	17	2 26 *	21	3 10 †
Illusions	37	2 93 †	17	1 41	21	1 30
Ambiguous Figures	37	2 25 ‡	17	0 08	21	2 00 ‡
Fluctuation Figures	28	0 45	16	0 14	18	2 04 ‡
Gottschaldt 8′ (R-W)	36	2 72 †	17	1 69	21	1 56
Gestalt Completion	35	1 75 ‡	15	2 51 *	20	2 55 †

* Statistical significance at a 0 02 level
† Statistical significance at a 0 01 level

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Concept Formation	37	2.32 *	17	2 26 *	21	3.10 †
Illusions	37	2 93 †	17	1 41	21	1 30
Ambiguous Figures	37	2 25 ‡	17	0 08	21	2 00 ‡
Fluctuation Figures	28	0 45	16	0 14	21	2 04 ‡
Gottschaldt 8′ (R-W)	36	2 72 †	17	1 69	18	1 56
Gestalt Completion	35	1 75 ‡	15	2 51 *	20	2 55 †

TABLE 7-15. WECHSLER-BELLEVUE INTELLIGENCE SCALE: SIGNIFICANCE OF GROUP MEAN DIFFERENCES BETWEEN NONOPERATIVE AND PREOPERATIVE RHEUMATIC AND NONRHEUMATIC HEART DISEASE PATIENTS *

Test	M_{rh}	M_{nrh}	*df*	*t*
Information	10.2	11.0	76	1.04
Comprehension	10.2	11.4	74	1.49
Digit Span	8.1	8.5	76	0.46
Arithmetic	9.0	9.4	76	0.27
Similarities	10.4	10.7	74	0.36
Picture Completion	10.1	10.9	76	1.08
Block Design	10.3	10.7	76	0.51
Digit Symbols	9.5	9.7	76	0.25
Verbal I Q.	103.3	106.3	76	0.76
Performance I Q.	110.8	111.9	76	0.28
Full-scale I.Q.	107.5	109.8	76	0.58

* This table is based on three more patients than the rest of the tables (N = 78). The three patients were subsequently dropped because of shifting medical diagnoses.

M_{rh} = mean for rheumatic heart disease group; M_{nrh} = mean for nonrheumatic heart disease group.

A comparison of nonoperative rheumatic patients with nonoperative nonrheumatic patients, as well as a comparison of the nonoperative rheumatic patients with preoperative rheumatic patients, was made by means of the *t* test and showed no significant differences on any of the Wechsler-Bellevue measures. Since no differences between the rheumatic and nonrheumatic patient groups have been found preoperatively, any differences beyond chance expectancy that might occur in the immediate postoperative retest may be expected to be related in some way to the surgical intervention.

It is evident from Table 7-16 that *significant psychologic impairment occurs following commissurotomy, as opposed to nonrheumatic heart operations.* Five of the eleven measures on the Wechsler-Bellevue scale show a significant deficit in the performance of the post-commissurotomy patients in comparison with the nonrheumatic operated heart patients in the immediate postoperative recovery period This deficit is mainly due to the failure of mitral commissurotomy patients to increase their preoperative scores when being retested with the same instrument after 3 to 4 weeks. Evidently, learning ability becomes impaired The actual tasks in which the impairments occur provide a clue to the type of psychologic functions involved.

The most consistent and persisting discrepancy in group mean scores is evident in Block

TABLE 7-16 WECHSLER-BELLEVUE INTELLIGENCE SCALE: SIGNIFICANCE OF GROUP MEAN DIFFERENCES BETWEEN RHEUMATIC (COMMISSUROTOMY) AND NONRHEUMATIC SURGICAL GROUP POSTOPERATIVE RETESTS 1, 2, 3, AND 4

Test	*Postop 1*		*Postop. 2*		*Postop. 3*		*Postop. 4*	
	df	*t*	*df*	*t*	*df*	*t*	*df*	*t*
Information	37	0.67	16	1.19	21	0.75	10	1.15
Comprehension	36	2.10 *	16	0.89	21	0.54	10	1.72
Digit Span	37	0.95	16	0.36	21	1.23	10	0.21
Arithmetic	37	0.41	16	0.23	21	0.99	10	0.09
Similarities	36	0.83	16	1.78	21	1.36	10	1.74
Picture Completion	37	1.66	16	0.12	21	1.02	10	2.38 †
Block Design	37	2.26 †	16	2.73 ‡	21	1.71 *	10	2.37 †
Digit Symbols	37	1.70 *	16	2.35 †	21	1.24	10	0.73
Verbal I Q.	37	1.04	16	0.89	21	1.07	10	1.14
Performance I Q	37	2.37 †	16	1.67	21	1.68	10	1.37
Full-scale I Q	37	1.85 *	16	1.27	21	1.45	10	1.23

* The difference between group means is statistically significant at a 0.05 level of significance.

† Statistical significance at a 0.02 level.

‡ Statistical significance at a 0.01 level.

All *t* tests are based on a one-tailed test of hypotheses, and all significant differences are in the expected direction, that is, the commissurotomy group's score is lower.

missurotomy patients, and their *implications* for medical management and rehabilitation of the patient, have been discussed by Priest et al (1957).

In analyzing the results obtained during the first 2 years of our study, Priest stated

> No effect could be ascribed to hypothermia in these *patients In so far as* the factors of prolongation of the effects of anesthetic, total duration of systolic blood pressure below 85 during operation and cardiac arrhythmias were concerned, they were more severe as a rule, in the nonmitral patients. The only consistent surgical difference is that in operations on the mitral valve there are always several periods of 15 to 30 seconds each when no blood is flowing from the left atrium to the left ventricle These are the periods when the surgeon's finger is occluding the mitral orifice It *is also the practice of some surgeons to compress* the carotid arteries during some of the intracardiac manipulations This was done in some, but not in all, of the mitral cases *in our group The* possible significance of this as a factor in the immediate post-operative signs of cortical involvement requires further study.

Suggestive histologic evidence of cortical *involvement due to persistence of rheumatic* fever in rheumatic heart patients has been presented by Bruetsch (1952). The impact of *stagnant hypoxia* upon the functions of the central nervous system has been emphasized by Pollock (1958). *Studies concerned with cerebral embolization* resulting from rheumatic endocarditis, bacterial endocarditis, and the general problem of cerebral emboli originating from the heart valves and cardiac chambers have been reviewed by *Askey* (1957), and Murphy (1954), and others A report on the neurologic, psychologic, and psychiatric aspects of cerebrovascular accidents encountered in the author's study leaves little doubt that cerebrovascular accidents *accompanying* mitral commissurotomy are a contributing factor to the observed disturbances in psychologic functions.

In view of these findings, the clinically observed frequent psychiatric *disturbances in* patients undergoing mitral commissurotomies *do not* appear to be of a purely functional nature, such as schizophrenic reactions or depressive states are frequently assumed to be. Rather, the psychiatric problems in the rheumatic heart patient may be triggered off by *the disruption of certain psychologic* functions which appear to be related to *organic changes* in the course of the heart disease and mitral valve surgery. As a high level of anxiety appears to be characteristic of cardiac conditions *in general, the additional stresses produced by* disruptions in perceptual and intellectual functions in mitral stenosis patients may noticeably increase the incidence of psychiatric disturbances. Depending upon the individual patient's personality make-up and ego resources determining his ability to withstand stressful situations, psychiatric complications may arise and take on various forms and intensities.

It is important to be aware of the considerable ability of most individuals to compensate for disruption of mental functions and to maintain a mental integrity and a reality orientation even under conditions of prolonged and relatively severe impairment. Consequently, only the psychologically most vulnerable of the mitral stenosis patients would be expected to develop psychoses.

The rehabilitative efforts of the postcommissurotomy patient, however, are undoubtedly influenced by the psychologic complications related to the course of his disease and surgery and require special efforts on his behalf in order to achieve and to maintain a general level of functioning commensurate with the high expectations based on a successful surgical correction of his mitral valve.

TABLE 7-17. ORGANIC TEST BATTERY: SIGNIFICANCE OF GROUP MEAN DIFFERENCES BETWEEN RHEUMATIC AND NONRHEUMATIC NONOPERATIVE AND PREOPERATIVE HEART DISEASE PATIENTS

Test	M_{rh}	M_{nrh}	*df*	*t*
Concept formation	4.0	4.2	69	0.86
Illusions	10 2	10.8	71	1.70 *
Ambiguous Figures.	13.0	18.2	69	1.34
Fluctuation Figures	86.1	89.0	60	0.16
Gottschaldt 8′ (R-W)	37.5	48.3	66	2.02 *
Gestalt Completion	28.4	37 8	63	2.00 *

* Significance at a 0 05 level. All significant differences are in the predicted direction· rheumatics have lower group mean scores.

tients and also with the preoperative nonrheumatic cardiacs. The nonoperative rheumatics, in turn, were independently compared with the nonoperative nonrheumatic cardiacs.

No differences were found between the two nonoperative groups.[1] The rheumatic patients about to undergo mitral commissurotomy, however, showed significant impairment on Standard Illusions and Ambiguous Figures when compared with the nonoperative rheumatic heart patients (The differences were significant at a 0.05 level of significance.) The Gottschaldt Figures and Street Gestalt Completion test did not reach statistical significance between the two rheumatic cardiac groups.

[1] This *t* test is based on 22 rheumatic cardiac and 7 nonrheumatic cardiac patients

It is apparent from Table 7-18 that the group mean scores on two cortical tests, the Standard Illusions and the Ambiguous Figures, as well as scores on the Gottschaldt Figures and the Gestalt Completion test, are significantly low in the commissurotomy patients in their immediate preoperative state as compared with the nonrheumatic cardiacs expecting heart surgery.

As the nonoperative rheumatic and nonrheumatic cardiacs did not differ from each other, it would seem that certain perceptual dysfunctions are characteristic of those patients in our study who were selected for a surgical correction of the mitral valve.

It should be noticed in this context that the Concept Formation test did not differentiate the commissurotomy candidates from the other cardiac groups, neither did the Fluctuating Figures. Consequently, an evaluation of the immediate preoperative perceptual disturbances of the commissurotomy patients has to be based only on those tests which indicate some deficit.

The observed low group mean scores appear to be related to specific areas of impairment and reflect difficulties in organization of visual-perceptual material involving productivity, perceptual flexibility, and ability to achieve meaningful closure. To the extent that the above tests measure what they are sup-

TABLE 7-18 ORGANIC AND PERCEPTUAL MEASURES SIGNIFICANCE OF GROUP MEAN DIFFERENCES BETWEEN COMMISSUROTOMY PATIENTS AND NONRHEUMATIC HEART SURGERY PATIENTS. PREOPERATIVE TEST

Measure	M_{com}	M_{nrs}	*df*	*t*
Concept Formation	4 0	4.3	43	0 75
Illusions	9 9	11.5	43	3 77 *
Ambiguous Figures	11 2	17 3	42	1 89 †
Fluctuation Figures	85 0	94 1	37	0 37
Gottschaldt 8′ (R-W)	39 5	53 4	40	2 21 ‡
Gestalt Completion	28.7	37.6	38	2.01 †

* ..

dit

M_{com} = mean for commissurotomy group; M_{nrs} = mean for nonrheumatic heart surgery group.

PART 8

Viral, bacterial, mycotic, and parasitic heart disease

gists tend to agree on the validity of the Wechsler-Bellevue Intelligence Scale, although their interpretations of the various subscales may differ; experimental validation of individual subscale meanings is still scarce.

The perceptual tests which the author has employed have been in use for many years, but are still not sufficiently validated experimentally. They are mainly clinical instruments based on certain theoretical considerations and clinical experience with various neurologic and psychiatric patients. Each of them is useful primarily in providing certain leads for the clinical psychologist as to the areas of mental functioning likely to be involved in a particular patient's mental difficulties, which the clinician then goes on to explore by means of clues derived from additional tests. It is for this reason that in this study as many as six such tests were included. Only in the light of cumulative evidence emerging from various types of test data is it possible to draw certain tentative conclusions at this stage of our knowledge of psychologic functions.

CONCLUSIONS OF THE PSYCHIATRIC STUDY

The results of the intellectual, perceptual, and concept formation tests employed in this study indicate that mitral commissurotomy is followed by impairments in psychologic functions reflected in these objective tests, when compared with nonrheumatic heart surgery patients.

Rheumatic as well as nonrheumatic cardiac patient groups have a tendency for impairment in Wechsler-Bellevue Digit Span, probably reflecting a generally high anxiety level

No differences in intellectual ability were observed between the nonoperative rheumatics and nonrheumatic heart patient groups

A comparison of mitral commissuratomy patients with nonrheumatic heart surgery patients preoperatively, three weeks after surgery, half a year, and during the second and third postoperative years, revealed that certain disturbances in intellectual functioning develop after mitral valve surgery. The initial postcommissurotomy disturbance in intellectual functions was widespread with significant differences in prorated performance I.Q. and full-scale I.Q., as well as in three specific subscales: Block Design, Digit Symbols, and Comprehension. Of these, only Block Design showed persistent significant differences after the 6-month postoperative retest. Consequently, there is noted improvement after an initial disruption of intellectual functions, although the disturbance does not remain confined to Block Design exclusively, as Similarities and Picture Completion also show tendencies toward impairment.

Results on a battery of organic tests, including a block-sorting type concept formation test, and five perceptual tests used clinically for evaluation of organic brain functions were presented. No differences were found between groups of nonoperative rheumatic and nonoperative nonrheumatic heart patients.

Two of three tests of the Yacorzynski battery for cortical involvement indicated that the mitral commissurotomy patients already had some impairments in the immediate preoperative period. The Gottschaldt Figures and the Street Gestalt Completion test gave similar results. There was no impairment on the Concept Formation test preoperatively.

Following heart surgery, the preoperative impairment on the perceptual tests persisted and, in addition, the Concept Formation test, not previously impaired, showed significantly lower scores for the commissurotomy group as compared with nonrheumatic surgical patients.

While the significantly lower scores of the commissurotomy group on the Concept Formation test and on the Gestalt Completion test persisted in all retests, there was a tendency toward recovery on the Standard Illusions and on Gottschaldt Figures. These findings suggest that while there is no evidence of initial differences between rheumatic and nonrheumatic heart patient groups in intellectual functioning, perceptual functioning, and problem-solving ability, some perceptual difficulties become apparent in the rheumatic cardiacs when their mitral valve disease requires surgical intervention. No such trend was evident in the nonrheumatic surgical candidates.

Following mitral valve surgery, impairments in intellectual functions and concept formation ability develop, in addition to the preoperative perceptual deficits. These latter changes appear to be associated with mitral commissurotomy.

Possible reasons for the observed disturbances in psychologic functioning of the com-

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1

Bacterial endocarditis

WALTER PRIEST AND EUGENE HILDEBRAND

INTRODUCTION

Bacterial endocarditis, a bacterial infection of the valves and lining of the heart, has been known by many names Among them are *endocarditis lenta, malignant endocarditis, septic endocarditis,* and *Osler's* or *Jaccoud-Osler's disease* An *acute,* a *subacute,* and a *chronic form* have been described in the voluminous literature

Basically, the disease process in all three is similar, varying, as one might expect, with the virulence of the infecting organism and with the resistance of the host. In the *acute form,* the organisms are sufficiently virulent to attack apparently healthy valves, and septic emboli much more often lead to metastatic abscesses than in the less acute types Little difference exists between the subacute and chronic varieties, and so the term "chronic" has largely been dropped, leaving only the "acute" and "subacute" types Even the latter distinction is gradually being discarded[1] Some recent reports in the literature have established *fungi* as the causative organisms

It seems quite logical that this disease should be known as "infectious endocarditis" (Jaccoud), or perhaps better still, as Keefer suggests, endocarditis should be classified etiologically and anatomically and not as "acute" or "subacute"

Essentially the same pathologic condition sometimes exists in the pulmonary tree, and occasionally also in the peripheral arteries. When the infection occurs in the pulmonary tree, it most often affects the *pulmonary artery or one of the principal branches,* but it has been noted to attack even the second and third branches leading into the pulmonary parenchyma itself. The process sometimes occurs in a patent ductus arteriosus, and occasionally in peripheral arteries, especially at the sites of arteriovenous fistulas. This "arteritis," however, can produce general pathologic findings just as if the lesions were located within the heart itself. Confusion in diagnosis can result. Essentially similar local pathologic findings are noted in these lesions as in the cardiac lesions, but often the treatment is different in that the lesions may be available to surgical approach

The term "endocarditis" has been criticized in that this disease most often attacks the valves of the heart and leaves the mural endocardium untouched. This, however, is not always the case Sometimes the disease process spreads from the valves to the mural endocardium, and occasionally it may begin on the mural endocardium itself The criticism may have its origin in the belief by some that the valves are not true endocardium However, since they are entirely covered by endocardium in their normal state, and since embryologically they form from the endocardium and do not contain myocardial fibers, they should be regarded as a portion of the endocardium Therefore, the term endocarditis is justified when referring to lesions, not only of the mural endocardium, but also of the valves.

[1] Because of the marked difference in response to therapy, classification into "viridans" and "non-viridans" endocarditis has been proposed. At present, the term "bacterial endocarditis" seems the most appropriate

hend why they attack the endocardium. Do they lodge on the surface, attacking from there, or are they brought to the subsurface by small blood vessels and attack from below? Is the heart that is being attacked "normal" or "abnormal"? Let us examine this last question first

In most instances the endocarditis is superimposed upon an already damaged heart. The damage can be *congenital* or *acquired.* The most common acquired cardiac damage leading to endocarditis is that caused by *rheumatic fever* Damage due to arteriosclerosis is a poor second. Syphilis as the underlying pathologic cause is rare, usually it affects the aorta and not the endocardium or valves per se Several series of cases reveal that a history of rheumatic fever or other rheumatic manifestations was found in approximately 50 per cent of all patients with endocarditis Other series showed that antecedent rheumatic disease was present in 80 per cent or more

The acute form of the disease is generally thought to occur on previously healthy valves, but rheumatic damage may have been present in some of the acute cases Further, since many of the acute cases occur following *acute sepsis* (as in those originating after a criminal abortion), it is most difficult to state with any degree of certainty that the valves were "normal" when the endocarditic process commenced It seems much more logical to believe that the antecedent septic process itself caused injury to the endocardium

Statistics as to the number of patients with rheumatic cardiac disease who subsequently develop endocarditis range from 4 to 30 per cent In studying autopsy material from patients residing in the Rocky Mountain region of the United States, the authors have been impressed by the high incidence of rheumatic valvular involvement Some of this was extensive and was the primary cause of death, as might be expected This percent has not exceeded the percentage for the remainder of the country, standing at about 5 per cent of the autopsy material Most of the rheumatic involvement that is found is minimal in extent and does not significantly interfere with cardiac function

In older people, it is sometimes exceedingly difficult to differentiate pathologically between minimal rheumatic valvulitis and that due to arteriosclerosis. Very few cases of *arteriosclerotic valvulitis* with superimposed endocarditis have been reported in the literature. It is apparent, however, that *limited coronary blood f*[illegible] lead to degenerative endocardial [illegible] farction can act as a *focus for bacterial endocarditis, but it is surprising* that this occurs so rarely in the light of the relatively large numbers of cases. Neither of the authors has seen an instance in which it has occurred. Again, it is difficult to exclude the presence of coexisting rheumatic valvular involvement. The authors have seen no cases of endocarditis in which *syphilis* could be regarded as the sole underlying etiologic factor.

Congenital heart disease is frequently the antecedent pathologic condition in bacterial endocarditis. A relatively small percentage of the general population, however, suffers from congenital heart disease compared to that which suffers from varying degrees of rheumatic carditis. However, when the number of patients with congenital lesions who subsequently develop endocarditis is considered, the picture is entirely different. Some series of cases indicate that a very high percentage die of this disease In studying the reported cases of congenital heart disease with endocarditis, one is impressed by the relatively large number in which *bicuspid aortic valves* and *interventricular septal defects* were the underlying pathologic conditions

Altered hemodynamics, especially alteration of direction of flow, over a long period of time could cause endocardial damage and possibly *subendocardial hyalinization.* Even a slight deviation of blood flow can produce changes in hemodynamics, although such changes may not produce symptoms *Arteriosclerotic valve changes* no doubt also cause similar changes in hemodynamics, and yet endocarditis is rarely seen in *uncomplicated* arteriosclerotic heart disease Perhaps this alteration in hemodynamics is not the entire answer. Some authors believe that rheumatic valvulitis always precedes endocarditis In the authors' cases, a history of rheumatic fever can be elicited in the majority Allen stated that it is not in the areas of eddy or at the coapting surfaces of the valve that the disease begins. He stated that, in valvular deformity, flowing blood is

gulfed by enlarged endothelial cells, following which the endothelial cells became necrotic and the surface of the endothelium was disrupted. Fibrin was laid down in these areas, thus protecting the bacteria from phagocytes of the circulating blood.

Host resistance, represented by partial immunity, probably plays a role in the pathogenesis of bacterial endocarditis This concept will be discussed in more detail in the section of Bacteriology, below.

In summary, two main factors must be considered in the pathogenesis of this disease. (1) previous cardiac damage and (2) implantation of bacteria, together with the possible factor of host resistance The reasons for the exceptionally high occurrence of antecedent rheumatic fever are still somewhat obscure The actual mode of implantation of the bacteria is probably via platelet thrombi or damaged endothelial cells, but possibly also via the blood vessels of the valve itself Perhaps both of these modes are involved

BACTERIOLOGY

Alpha hemolytic streptococcus is found in 70 to 80 per cent of the positive cultures obtained This is the organism commonly cultured from extracted teeth and from blood cultures following tonsillectomy Most strains are green producing on blood agar (*Streptococcus viridans*) As a common inhabitant of the mouth and respiratory tract, it is regarded as nonpathogenic It is a fairly common contaminant in the bacteriology laboratory, but when the organism is found in blood cultures, it is seldom a contaminant The list of other bacteria and microorganisms causing this disease is long, and new organisms are constantly being added to it Jones (1950) collected the following list from the literature

MICROORGANISMS FOUND IN BACTERIAL ENDOCARDITIS

Micrococcus—29
  (*Aureus, albus, citreus*)
Neisseria gonorrhoeae—42
  Meningitides—15
  Catarrhalis, flava, pharyngis, perflava—10
Gram-negative enteric group—19
Paracolon bacillus
Escherichia coli
Salmonella
  (*Schottmulleri, choleraesuis, typhosa, typhimurium*)
Klebsiella pneumoniae
Corynebacterium—3
  (*Diphtheriae*)
  (*Haemolyticum*)
  (*Diphtheriticum*)
Mycobacterium tuberculosis—8
Actinomyces—6
  (*Bovis*)
  Graminis
  Septicus
Treponema—3
Brucella—15
  (*Abortus, melitensis, suis, bronchiseptica*)
Haemophilus influenzae—17
  (*Parainfluenzae, aphrophilus*)
Diplococcus pneumoniae—19
Spirillum minus
Streptobacillus moniliformis (*Haverhillia*)
Lactobacillus
Actinobacillus lignieresii
Clostridium perfringens (*welchii*)
Erysipelothrix rhusiopathiae
Nocardia
Histoplasma capsulatum
Candida (*Monilia*)
  (*Albicans, parakrusei, guillermondi*)
Diplococcus crassus
Grahamella
Veillonella gazogenes
Pasteurella tularensis
Dialister

SOURCE From Jones, 1950.

Since Jones' article, the following organisms have been reported as causing one or more cases of bacterial endocarditis

Actinomyces muris
Candida
  (*Krusei, neoformans*)
Leptothrix
Herrellea vaginicola

Fungi have also been recovered as the only organism When these appear as the only organism in blood cultures, they should *not* be dismissed categorically as contaminants.

Jones included the tubercle bacillus and the treponema as causative organisms in bacterial endocarditis When these organisms occur in the heart valves, they are almost always part of a generalized infection or, in the case of syphilis, a gummatous process.

In one series of 16,000 autopsies, a single instance of primary tubercle bacillus endocarditis was found (Mark, quoted by Russell et al.). Con-

HISTORY

Kerr (1955), in his monograph, gives a review of the history of endocarditis, dating back to 1554. Clinical descriptions made long ago can be interpreted in the light of present knowledge as examples of this disease. Advances in the knowledge of infectious diseases due to bacteria (Pasteur), the circulation of the blood (Harvey), and embolism (Virchow), combined with astute clinical observations, finally led to the establishment of bacterial endocarditis as a disease entity. Osler became convinced that the disease was of bacterial origin His Gulstonian lectures (1885), in which he analyzed 209 cases, served to disseminate knowledge about endocarditis and to stimulate clinical, bacteriologic, pathologic, and experimental observations relative to this disease. Jaccoud studied the disease both clinically and bacteriologically, and other French investigators cited other examples German researchers also described this condition, and the use of blood cultures became fairly common in Germany in the 1890s. For several years following this, the use of blood cultures increased Investigators both in America and abroad added significantly to the clinical and bacteriologic aspects of the disease. However, most investigators were discouraged by the uniformly poor results of treatment. Numerous organisms (see Bacteriology, below) were isolated from blood cultures However, it was not until the advent of penicillin (1943) that rapid progress began in the clinical management of endocarditis and led to our present-day concepts of the bacteriology, pathology, and clinical management of this disease

PATHOGENESIS

The primary lesion in this disease is a bacterial (or other microorganismal) inflammatory process involving the valves or lining of the heart. Obviously, then, the causative organisms must gain access to the blood stream in order to be carried to the heart and must become implanted on or within the endocardium *Bacteremia* and *bacterial implantation* are, therefore, fundamental in the pathogenesis. Another factor, *host resistance*, is probably involved also. The localization of the infection and its duration in most cases indicate partial immunity of the host

Bacteremia. The term bacteremia· means, literally, the presence of bacteria in the blood, but implies also that there are no untoward symptoms or signs resulting therefrom. It is the opinion of most investigators that bacteremia must occur in all people, aften in the course of normal living. Many varieties of bacteria are present on the skin and in the mouth, respiratory tract, and genitourinary system, and in fact are regarded as "normal inhabitants" in these areas. Most of them, when they enter the blood stream by way of a cut or abrasion, do so in small numbers, find no suitable place for growth, and are quickly destroyed by the defenses of the body. However, in the case of incision and drainage of an abscess, tonsillectomy, tooth extraction, or operation on the genitourinary system, large numbers of bacteria could be "injected" and, if proper conditions prevail, could become implanted within the heart Often, a history of pharyngitis or upper respiratory infection can be elicited. Bacteremia may occur as a result of genitourinary instrumentation, bronchoscopy, and proctoscopy.

In approximately 40 per cent of the cases, the portal of entry of the offending organism cannot be demonstrated. The *teeth* furnish the most common portal of entry (about 45 per cent). Dental sepsis, caries, and tooth extraction are usually at fault. However, transient *Streptococcus viridans* bacteremia has been demonstrated in individuals having no dental sepsis. *Upper respiratory infections* are the next most common precursors *Pregnancy, puerperium*, and *criminal abortion* account for about 6 per cent. *Direct injection* of contaminated material into a vein by drug addicts has led to endocarditis. In these cases, the tricuspid valve is usually involved, a rare occurrence otherwise. *Surgical operations within the heart*, whether for acquired or congenital lesions, have been followed by endocarditis in 1 to 2 per cent of cases (Koiwai and Mahas; Finland).

Even though the elapsed time (3 to 6 months) in some of the reported cases makes surgery questionable as the responsible procedure, in the majority of cases there can be no doubt. Apparently the causative organism need not be on the surgeon's hands, instruments, etc., at the time of operation An occasional case has occurred following *cardiac catheterization* The authors have treated a patient who developed the disease following transurethral resection.

Implantation. It is easy to understand how bacteria can gain entrance to the blood stream, but it is somewhat more difficult to compre-

gulfed by enlarged endothelial cells, following which the endothelial cells became necrotic and the surface of the endothelium was disrupted Fibrin was laid down in these areas, thus protecting the bacteria from phagocytes of the circulating blood.

Host resistance, represented by partial immunity, probably plays a role in the pathogenesis of bacterial endocarditis This concept will be discussed in more detail in the section of Bacteriology, below.

In summary, two main factors must be considered in the pathogenesis of this disease. (1) previous cardiac damage and (2) implantation of bacteria, together with the possible factor of host resistance. The reasons for the exceptionally high occurrence of antecedent rheumatic fever are still somewhat obscure. The actual mode of implantation of the bacteria is probably via platelet thrombi or damaged endothelial cells, but possibly also via the blood vessels of the valve itself. Perhaps both of these modes are involved.

BACTERIOLOGY

Alpha hemolytic streptococcus is found in 70 to 80 per cent of the positive cultures obtained This is the organism commonly cultured from extracted teeth and from blood cultures following tonsillectomy Most strains are green producing on blood agar (*Streptococcus viridans*) As a common inhabitant of the mouth and respiratory tract, it is regarded as nonpathogenic It is a fairly common contaminant in the bacteriology laboratory, but when the organism is found in blood cultures, it is seldom a contaminant The list of other bacteria and microorganisms causing this disease is long, and new organisms are constantly being added to it. Jones (1950) collected the following list from the literature

Microorganisms Found in Bacterial Endocarditis

Micrococcus–29
 (*Aureus, albus, citreus*)
Neisseria gonorrhoeae–42
 Meningitides–15
 Catarrhalis, flava, pharyngis, perflava–10
Gram-negative enteric group–19
Paracolon bacillus
Escherichia coli
Salmonella
 (*Schottmulleri, choleraesuis, typhosa, typhimurium*)
Klebsiella pneumoniae
Corynebacterium–3
 (*Diphtherae*)
 (*Haemolyticum*)
 (Diphtheriticum)
Mycobacterium tuberculosis–8
Actinomyces–6
 (*Bovis*)
 Graminis
 Septicus
Treponema–3
Brucella–15
 (*Abortus, melitensis, suis, bronchiseptica*)
Haemophilus influenzae–17
 (*Parainfluenzae, aphrophilus*)
Diplococcus pneumoniae–19
Spirillum minus
Streptobacillus moniliformis (*Haverhillia*)
Lactobacillus
Actinobacillus lignieresii
Clostridium perfringens (*welchii*)
Erysipelothrix rhusiopathiae
Nocardia
Histoplasma capsulatum
Candida (*Monilia*)
 (*Albicans, parakrusei, guillermondi*)
Diplococcus crassus
Grahamella
Veillonella gazogenes
Pasteurella tularensis
Dialister
 SOURCE From Jones, 1950.

Since Jones' article, the following organisms have been reported as causing one or more cases of bacterial endocarditis.

Actinomyces muris
Candida
 (*Krusei, neoformans*)
Leptothrix
Herrellea vaginicola

Fungi have also been recovered as the only organism. When these appear as the only organism in blood cultures, they should *not* be dismissed categorically as contaminants

Jones included the tubercle bacillus and the treponema as causative organisms in bacterial endocarditis. When these organisms occur in the heart valves, they are almost always part of a generalized infection or, in the case of syphilis, a gummatous process.

In one series of 16,000 autopsies, a single instance of primary tubercle bacillus endocarditis was found (Mark, quoted by Russell et al.). Con-

HISTORY

Kerr (1955), in his monograph, gives a review of the history of endocarditis, dating back to 1554. Clinical descriptions made long ago can be interpreted in the light of present knowledge as examples of this disease. Advances in the knowledge of infectious diseases due to bacteria (Pasteur), the circulation of the blood (Harvey), and embolism (Virchow), combined with astute clinical observations, finally led to the establishment of bacterial endocarditis as a disease entity. Osler became convinced that the disease was of bacterial origin His Gulstonian lectures (1885), in which he analyzed 209 cases, served to disseminate knowledge about endocarditis and to stimulate clinical, bacteriologic, pathologic, and experimental observations relative to this disease. Jaccoud studied the disease both clinically and bacteriologically, and other French investigators cited other examples German researchers also described this condition, and the use of blood cultures became fairly common in Germany in the 1890s. For several years following this, the use of blood cultures increased. Investigators both in America and abroad added significantly to the clinical and bacteriologic aspects of the disease. However, most investigators were discouraged by the uniformly poor results of treatment Numerous organisms (see Bacteriology, below) were isolated from blood cultures However, it was not until the advent of penicillin (1943) that rapid progress began in the clinical management of endocarditis and led to our present-day concepts of the bacteriology, pathology, and clinical management of this disease.

PATHOGENESIS

The primary lesion in this disease is a bacterial (or other microorganismal) inflammatory process involving the valves or lining of the heart Obviously, then, the causative organisms must gain access to the blood stream in order to be carried to the heart and must become implanted on or within the endocardium *Bacteremia* and *bacterial implantation* are, therefore, fundamental in the pathogenesis. Another factor, *host resistance*, is probably involved also. The localization of the infection and its duration in most cases indicate partial immunity of the host

Bacteremia. The term bacteremia means, literally, the presence of bacteria in the blood, but implies also that there are no untoward symptoms or signs resulting therefrom. It is the opinion of most investigators that bacteremia must occur in all people, aften in the course of normal living. Many varieties of bacteria are present on the skin and in the mouth, respiratory tract, and genitourinary system, and in fact are regarded as "normal inhabitants" in these areas. Most of them, when they enter the blood stream by way of a cut or abrasion, do so in small numbers, find no suitable place for growth, and are quickly destroyed by the defenses of the body. However, in the case of incision and drainage of an abscess, tonsillectomy, tooth extraction, or operation on the genitourinary system, large numbers of bacteria could be "injected" and, if proper conditions prevail, could become implanted within the heart. Often, a history of pharyngitis or upper respiratory infection can be elicited. Bacteremia may occur as a result of genitourinary instrumentation, bronchoscopy, and proctoscopy.

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rates tend to inhibit growth of the more fastidious organ[illegible] of the media should be done [illegible] sample [illegible] tory for inoculation. This results in a lower per- centage of positive cultures. Saponin should be added to the media to destroy the leucocytes in the blood Otherwise, phagocytosis of bacteria and prevention of their growth may occur.

The materials necessary at the bedside include two sterile Petri dishes, two tubes of nutrient agar previously melted and cooled to approximately 45°C [illegible] kept in this condition by means of hot [illegible] late broth, and a tube of Sabouraud's medium are also included In selected cases, the Castanoga bottle (Brucella) is also used Becton-Dickinson prepared media in evacuated containers are quite satisfactory, especially since they have added 10 per cent carbon dioxide They are also supplying prepared Castanoga bottles The liquid medium is warmed prior to inoculation This eliminates the growth lag and possibly prevents destruction of some of the more sensitive organisms Approximately 1 ml of blood is added to each of the two tubes of melted agar, and they are replaced in the thermos bottle containers Approximately 0 5 ml is added to the Sabouraud's slant. Then 1 ml is placed in the thioglycolate broth and the remainder, approximately 3 ml each, in the Kracke's medium and the trypticase–soy broth. If the Castanoga bottle is used, approximately 2 ml more of blood is required When all the media has been inoculated, the pour plates are made, using the two Petri dishes brought for that purpose

Incubation in the laboratory is at 35°C rather than at 37°C The authors' experience on this point is in agreement with the findings of the Communicable Disease Center in Atlanta, Georgia. Likewise, it has been found unnecessary to flame the edges of the Petri dishes and the lips of the test tubes In the laboratory, one of the pour plates is incubated aerobically and the other anaerobically Approximately 10 per cent carbon dioxide is added to the bottle containing the trypticase–soy broth Greater attention is paid to the possible presence of the anaerobes in approximately 2 of the 10 cultures taken In two others, less different media are used, and the percentage inoculum is increased In all instances, of course, if there is an obvious possible source of introduction of bacteria into the blood stream, appropriate cultures are taken from these sources In case of suspected endocarditis in a known drug addict, the possibility that the microorganism is a fungus is considered, and appropriate changes are made in the media. This procedure is also carried out at a later date if preliminary cultures are negative and the clinical picture continues to warrant a search for bacteremia.

In about 20 per cent of all cases of proved endocarditis, blood cultures will be negative in spite of most careful work. In part, this is due to lesions occurring on the right side of the heart, with bacteria being present in the pulmonary circulation but being destroyed before reaching the general circulation. Also, bacteria may be destroyed in the general circulation almost immediately upon being released from the involved valve. In some cases, organisms are found at postmortem examination when blood cultures had been negative during life This was true of 6 of the 11 patients of Cates and Christie, who showed persistently negative blood cultures. Cultures should not be discarded as negative until after 28 days.

When a positive culture is obtained, it is essential that the sensitivity of the organism be determined It is important that the bactericidal (not merely bacteriostatic) level of the antibiotic be determined The serial-dilution technique is used. The authors have found the disk technique to be completely unsatisfactory in bacterial endocarditis work Adequate control to check the potency of the antibiotic should always be undertaken. This is best accomplished by utilizing an organism with a known sensitivity Such organisms may be kept in the laboratory for this express purpose It is impossible on the first serial dilution to determine whether the organism has been killed or merely arrested in growth Subcultures are necessary to determine the concentration necessary to kill the organism

Antibiotic assays are likewise necessary during therapy to make sure that the concentration of the antibiotic in the blood is adequate for control of the infection. Blood is drawn from the patient just prior to a given dose of the antibiotic The serum is used in serial dilutions to which is added the organism originally obtained from the patient Better still, two dilution series are set up, using the patient's organisms in one and the standard organisms maintained in the laboratory in the other. In addition, the authors have found it necessary to cross-check with a control serum drawn from a healthy person. Another control is prepared by utilizing known dilutions of the antibiotics The level of the antibiotic in the patient's blood should be substantially higher than that necessary to kill the organisms. It is also possible, utilizing the serial-dilution technique, to determine various combinations of antibiotics which can best be utilized in the specific case in question.

Technically, it may be difficult to determine

in contact with the valvular surface for a longer time than in normal hearts. *He believed that one reason for the small number of cases occurring in patients with atrial fibrillation is the lack of a presystolic jet of blood striking the atrial surface of the mitral valve.*

In order to produce bacterial endocarditis in the experimental animal, two factors are needed. One of them is *injury* to the lining of the heart, the other is *repeated injections of bacteria.* The acute form has been produced relatively easily, but it is much more difficult to produce the chronic or subacute form. Injection of the pathogenic bacteria must occur soon after the injury to the endothelium, apparently before endothelial regeneration has occurred to protect the valve from bacterial invasion.

The effects of *stress* on the endocardium itself, leading to increased susceptibility to infection, has been postulated as the cause of endocarditis. Highman and Altland subjected rats to high altitudes. They noted fibrinous swelling of the endocardium, the lesions occurring predominantly on the valves of the left side of the heart These animals were then injected with organisms obtained from patients with bacterial endocarditis, and 66 per cent of them developed the disease at the site of the endothelial lesions Injections of the same organisms into rats which were not subjected to high altitude resulted in bacterial endocarditis in only 1 out of 39 experimental animals.

This stress factor may explain the relatively large number of cases occurring in soldiers subjected to severely rigorous duty and possibly in the increased number of cases noted in postwar time. In these cases, it has been shown that there is an increase in the involvement of the aortic valve compared with that which one would expect under usual circumstances, and also there is a marked decrease in the history of previous rheumatic infection Angrist and Marquiss believe that three factors contribute to altering the collagen response of the heart valves, which in turn permit bacteria to become localized. These factors are *stress* (the effect on the adrenal cortical hormones would alter the reaction of collagen), *starvation* (alteration of the serum protein may diminish the immune response), and *aging* (this results in destroying the elasticity of the heart valves and rendering it more susceptible to trauma).

We have so far shown that, in most instances, previous damage to the endocardium is a prerequisite for the development of subsequent bacterial endocarditis. The exact mode of implantation of the infection is not known

Gross (1937) studied the blood supply to the endocardium and its relationship to bacterial endocarditis. He noted muscle slips which contained blood vessels leading to the aortic and mitral valves. He concluded that *normal human heart valves are not vascularized to a significant degree* Harper showed that the cat, dog, sheep, goat, pig, and horse have blood vessels in the normal valves, whereas man, rabbits, and guinea pigs rarely have vascular valves. He showed that it was easier to induce bacterial endocarditis in those animals in which the valves were vascularized than in those with relative avascularity. The authors' studies on the heart valves of rheumatic fever patients have indicated that, in old healed valvular involvement, no increase in vascularity was present. It is known, however, that *in early rheumatic fever the valves are definitely vascularized.*

It is known that bacterial endocarditis occurs most frequently in the third decade, so perhaps in such persons avascularity of valves has not yet had time to occur. Many investigators feel that the initial vascularity persists. It is possible that recurring infections by the rheumatic process, which most clinicians believe to be the rule rather than the exception, could prolong the increased vascularity of the heart valves In one case of bacterial endocarditis (Hildebrand and Priest, 1947), bacteria within and surrounding a small blood vessel in an inflamed valve was noted This vessel was traced by serial sections. Bacteria appeared to be migrating from its lumen to the adjacent tissue

Osler considered the possibility of platelet thrombi on the valves at the site of subsequent bacterial endocarditis. Such thrombi could form a protection for bacteria against the phagocytes within the circulation and allow the process to gain a foothold. It is possible that the subendothelial portions could be injured in some way, then added strain placed upon the valves would disrupt the surface endothelial cells, cause the formation of platelet thrombi, and lead to implantation of bacteria at the surface. Grant et al. found that such platelet thrombi would remain uncovered by endothelium for approximately 2 days This was confirmed experimentally by Wyssokowitsch. The authors demonstrated bacteria within damaged endocardial cells without overlying platelet thrombi MacNeal et al. injected bacteria recovered from cases of bacterial endocarditis into rabbits at frequent intervals. Valvular lesions apparently began when bacteria were en-

myocardium are reported. In many cases, *Aschoff bodies* are found Bracht and Wachter injected rabbits with an alpha hemolytic streptococcus In some of these animals, they observed collections of lymphocytes in the myocardium. The name "Bracht-Wachter lesion" was given to these by Libman. Some authors believe that these lesions are specific for this form of bacterial endocarditis.

One-half to three-fourths of all cases show some type of *skin or mucous membrane lesion*, petechiae being the most common More than one type may occur simultaneously. While all occur relatively late, skin lesions may be the patient's presenting complaint In the terminal stage of an untreated case, the entire body may be covered with *petechiae* Whether petechiae are caused by minute emboli or represent altered capillary endothelial reaction is still debated The fact that they can be produced by the Rumple-Leede's test suggests increased capillary permeability Microscopically, they consist of minute hemorrhages surrounded by round cell infiltration *Splinter hemorrhages* in the nail beds are probably of similar origin Petechial hemorrhages in the retina can occur

The classic *Osler's nodes* are red, painful swellings usually occurring on the tips of fingers and toes They gradually become more dusky in color and disappear within a few days Microscopically, there is inflammatory polymorphonuclear infiltration of the capillary walls, with marked necrosis The inflammatory reaction may spread to adjacent nerves, thus probably accounting for the pain

Janeway first described the skin lesion which since has borne his name (*Janeway lesions*) It consists of numerous confluent small hemorrhages found on the palms of the hands and soles of the feet The surface is slightly nodular Microscopically, the lesions are similar to the Osler node, but the reaction is more acute They are not painful

Embolic phenomena occur sooner or later in almost all cases of untreated bacterial endocarditis They are a relatively late manifestation of the disease, but in approximately one-third of the collected cases, embolism was the presenting symptom Most of the emboli and resulting infarctions are of a nonsuppurative nature Approximately 10 per cent cause suppuration

The *spleen* is the most common internal organ showing evidences of embolic infarction. According to Fox, the upper pole is most commonly involved He also found follicular hyperplasia and slight increase in the reticuloendothelial activity. Suppuration was present in 5 of 25 cases. The *kidney* is the second most common site of internal embolic phenomena. Horder noted renal infarction or embolism in 98 of 162 cases. The term "flea-bitten kidney" describes the gross appearance of these kidneys quite well. Embolic manifestations in the glomeruli are common. *Diffuse glomerulonephritis* may occur alone or in combination with renal infarction. The embolic lesions seldom cause renal insufficiency, but the longer the course, the more frequent are the lesions of true glomerulonephritis, and these often result in renal failure.

One of the authors' earliest patients, who had had the disease for several weeks before successful treatment was instituted, developed *hypertensive cardiovascular disease* about 2 years after recovery from bacterial endocarditis There was no question about her being a normotensive individual prior to the endocarditis. Death occurred in the seventh postrecovery year due to calcific embolism of the left main coronary artery. The kidneys showed diffuse chronic glomerulonephritis and pyelitis

Central nervous system lesions are common. They are embolic in character In untreated patients, they usually occur late, but they may cause the presenting symptoms in a previously undiagnosed case. They have been known to occur during the course of antibiotic therapy, even after the vegetations of the valves have been sterilized *Meningitis* occasionally occurs.

Another embolic lesion is the *mycotic aneurysm* It is thought that this lesion is due to emboli in the vasa vasorum, with resultant inflammatory reaction, weakening of the wall, and outpouching Sometimes, when this type of lesion attacks an unprotected artery, such as one in the abdomen, the weakened wall may rupture and death ensue If the lesion occurs in a peripheral artery, well protected by fascia and muscle, the outpouching may become thrombosed and only local rupture occur.

These lesions seldom are the presenting symptom of the disease, but recently the authors saw a man 65 years of age who had a nonpulsating mass in the left groin Dissection of this mass,

sidering the frequent incidence of tubercle bacillus bacteremia, this is interesting. Russell adds a case of his own, in which tubercle bacilli, presumably from an old healed pulmonary lesion, became implanted on the sterile but unhealed vegetations remaining from a recent staphylococcus endocarditis. Disseminated miliary tuberculosis followed the propagation of the bacilli within the vegetations.

Mixed organisms have been reported. It is of great importance, if at all possible, to isolate the causative organism in this disease. It is only in this way that the duration of therapy and the choice of antibiotics may be determined. It is likewise important that therapy be not delayed because of the inability to secure a positive blood culture, for this is not obtainable in about 10 to 20 per cent of the cases. The patient who does not have a positive blood culture in the presence of this disease is at a serious disadvantage. It thus behooves the pathologist to exercise extreme care in the technique of blood cultures so that successful cultures may be obtained. It is likewise his responsibility to determine drug sensitivity, not only bacteriostatic but also bactericidal levels, and thus aid the clinician in the care of the patient After therapy has begun, it is necessary to make periodic bacterial assays in order to determine whether or not a sufficient amount of the antibiotic is present in the circulating blood of the patient

The finding of more than one organism in blood cultures must not lead to the conclusion that one is a contaminant, since *endocardial infection with more than one organism can occur.*

Blood Cultures.[2] In obtaining blood cultures, *it is of the utmost importance to withhold antibiotics until after the blood has been drawn.* If the patient has been on any antibiotic therapy including sulfonamides, such therapy should be discontinued before drawing blood for culture. Even a week's delay on this account will not jeopardize the patient as much as attempting to treat him blindly.

Adequate agents are available for counteracting the effect of most of the sulfa preparations and penicillin (PAS and penicillinase) but, as yet, none to counteract the effect of other antibiotics

[2] For technique of blood cultures, see also Part 4, Chap. 11. *Editor.*

The authors routinely incorporate antipenicillin and antisulfa materials in their cultures. The Communicable Disease Center in Atlanta, Georgia, has shown that these substances do not affect the growth of bacteria.

There has been much discussion in the literature regarding the best site for obtaining blood for culture, the number of cultures to obtain, the amount of blood to take in each instance, and the optimal time for securing the culture Blood taken from *arteries* has shown a slightly higher percentage of positive cultures than that taken from *veins.* However, if the arm is warmed, blood taken from the antecubital vein will show as many positive cultures as that taken from an artery. Occasionally, *cultures of bone marrow* will be positive when cultures of the peripheral blood are negative. In most instances, the first blood culture taken will be positive. The authors' routine is to make five cultures equally spaced throughout the first day and another five throughout the second day. Occasionally, repeated cultures over a long period of time may be necessary to secure a positive culture. Laboratories in different parts of the country use 1 to 20 ml of blood for each culture The authors believe that 1 ml is an inadequate sampling, that 20 ml is excessive, and have found that *10 ml of blood is quite adequate in most instances.* It has been shown that the bacteremia in bacterial endocarditis is a constant rather than an intermittent finding. The authors believe, then, that adequate sampling can be obtained in the first two days by taking blood at different times, regardless of the temperature curve

The use of *epinephrine* prior to drawing blood in order to dislodge bacteria from the spleen is a common practice in France, but actual proof of better results from this technique are lacking.

Preparation of the skin prior to venipuncture for blood culture is most important. The arm should be warmed by hot compresses. The site of venipuncture should be cleansed with one of the liquid soap preparations used for surgical scrub purposes, followed by painting with iodine, then washing with alcohol. All palpation of the venipuncture site should be done prior to preparing the arm. The needle and syringe, of course, should be adequately sterilized. If the vein is missed on the first attempt, the needle should be discarded and another one substituted.

Careful technique in the performance of the blood culture is of the utmost importance. This not only pertains to the careful handling of the blood specimen itself, but also to the preparation and handling of the various media necessary for the culture. As noted previously, 10 ml of blood is an adequate sample in most instances. Anticoagulants should not be used. Oxalates and cit-

a heart murmur develops where none was previously present, or a previously present murmur becomes intensified, or a new murmur develops, or the patient does not respond to treatment in the expected manner. Diagnosis will depend on the laboratory procedures referred to above and the finding of a positive blood culture.

TREATMENT

Historical. Perry (1936) stressed the ineffectiveness of therapy aimed at sterilizing the blood stream and was aware that the disease was "universally fatal not from any lack of resistance on the part of the patient but from the curiously isolated situation of the organisms in the thrombotic valvular vegetations, where they would appear to be immune from circulating antibodies." In effect, he was saying what later became obvious when the sulfonamides failed to cure the disease, although able to kill the bacteria in vitro, namely, that, to *be effective in this disease, a drug must have the ability to penetrate fibrin.* This ability the sulfonamides do not have while penicillin does, as was shown by Nathanson (1946) by means of tissue cultures Perry despaired of ever curing bacterial endocarditis except by preventing rheumatic fever Yet, in his own city, the antibiotic destined to change this hopelessness had been available for 7 years.

The earliest attempts to treat bacterial endocarditis with penicillin (during World War II) resulted in failure The average daily dosage was 40,000 to 60,000 units The limited supply then available was almost wholly requisitioned by the Armed Forces for treatment of pneumococcal, beta hemolytic streptococcal, staphylococcal, and gonococcal infections, in which brilliant success had been obtained with 40,000- to 60,000-unit daily dosage Because of this, no further attempt was made to treat bacterial endocarditis with penicillin until Loewe (1943) obtained apparent clinical cure in seven patients suffering from *Streptococcus viridans* endocarditis with daily doses of 250,000 units

Unaware of Loewe's investigations, one of the authors (Priest) had under treatment at the same time a patient in whom penicillin was being administered (by coincidence) in the same daily dosage and by the same continuous intravenous-drip method Previous administration of penicillin had generally been by intramuscular injection. During the many weeks of treatment of this patient, the daily dosage was increased for brief periods to 500,000 and, on two occasions, to 1,000,000 units. Although apparently improving clinically, the patient died of massive intestinal hemorrhage in the fifteenth week of penicillin treatment and the forty-fourth week of the disease.

Autopsy revealed almost complete healing of the valve, but in the valve substance, colonies of bacteria surrounded by inflammatory reaction were still present. Daily blood cultures and blood penicillin level determinations on this patient throughout the many weeks of treatment emphasized the fact that a blood penicillin level many times that necessary to inhibit the organism in vitro is necessary for cure of this disease. A daily dosage inadequate for cure always results in negative blood cultures and usually also in lowering of the temperature and in general clinical improvement. Partial healing of the edges of the valve with disappearance of vegetations can take place in the presence of inadequate dosage, but bacteria remain viable in quantity in the deeper portions of the valve.

As the result of Loewe's work, limited amounts of penicillin per patient were allocated to several centers throughout the country By the latter part of 1945 it became evident that penicillin, in daily dosage much in excess of that necessary for other susceptible diseases, was effective against alpha hemolytic (S viridans) endocarditis Not only was the active bacterial process arrested, but complete healing of the valve took place and the patients remained cured of the endocarditis

The authors' experience during this period coincided with that of other centers. When dealing with organisms killed in vitro by concentrations of penicillin ranging from 0 01 to 1.0 units per milliliter, a marked increase in the percentage of cures occurs when a daily dosage of 500,000 units by continuous drip is reached. This is greatly in excess of the amount necessary to sterilize the blood stream and keep it sterile. The excess serum concentration of penicillin is necessary because the concentration diminishes as penicillin diffuses through the fibrin barrier of the lesions. It became established that, in most cases, cure could not be effected unless a serum concentration of penicillin 4 to 10 times that required to kill the organism in vitro was maintained at all times.

A given daily dosage, even if administered by continuous intravenous drip, does not produce the same serum concentration in every patient. The rate of excretion, which is chiefly via the kidneys,

the sensitivity of anaerobic organisms. The authors have found most of these not to be complete anaerobes. Most of them will grow in thioglycolate broth. If this medium is used in the serial-dilution technique, not too much difficulty is encountered. If, however, the organisms will not grow satisfactorily in thioglycolate broth, evacuation of the air around the cultures and substitution of carbon dioxide may be necessary. Even in aerobic cultures, the addition of a small percentage of carbon dioxide in the surrounding atmosphere tends to enhance growth of the organisms

Further discussion of the antibiotic sensitivity and of the antibiotic assays in relation to therapy will be found below in the section on therapy.

PATHOLOGY

The lesions found in endocarditis can be divided into those of the lining of the heart itself and those found elsewhere in the body, due to either *embolic phenomena* or a *hypersensitivity reaction*. It is also pertinent to discuss the endocardial lesions found in cases treated with penicillin (Hildebrand and Priest, 1947).

The theories as to the mode of onset of endocarditis have been described. The lesions in the untreated state show essentially a necrotic core containing bacteria, over which there are successive layers of platelets and thrombi. The bacteria are relatively few in number near the surface and also in the deepest portion of the lesion. Perhaps this can best be explained by the fact that, in these areas, phagocytic activity of the leucocytes is most active The area of the valve which is involved by this thrombotic process shows a chronic, and sometimes subacute, inflammatory reaction, with fibroblastic proliferation and new blood vessel formation. Thus, there is not only an active inflammatory reaction present, but also a tendency toward healing The *friable* nature of the surface lesions renders them susceptible to fracture, with small pieces being broken off and forming *emboli*.

Sometimes the destructive process proceeds rather rapidly, in which instance there is more destruction of valve substance than when the inflammation is slow, as it usually is. Occasionally, the process is so necrotizing that the valve is ruptured, or there is rupture of one or more chordae tendineae. A few instances of spread of the infection from the aortic valve to the adjacent sinuses of Valsalva have been reported. *Aneurysm* and *rupture of a sinus* can follow. When the process is slow, the destructive forces are in part matched by the healing forces The protective layer of fibrin tends to protect the bacteria from leucocytes, thus enabling the former to reproduce.

Moore states that healing of these lesions occurs in five general steps: (1) a covering of fibrous tissue, (2) invasion of the layer of bacteria by phagocytes, (3) calcification of the bacterial colonies, (4) hyalinization and calcification of the core of the vegetation, (5) endothelialization of the spaces and clefts in the vegetation and over the surface. This process is essentially the same as that which the authors have observed. As the healing process continues, hyalinization and excessive calcification are produced. Thus, a *valve which has healed following bacterial endocarditis is more markedly deformed than it was prior to being attacked by the bacterial infection*. This finding was outstanding in the authors' cases

The frequency with which the different heart valves are involved parallels the valve involvement in rheumatic fever. Perry tabulated valvular involvement in a series of cases The mitral valve was the site of the disease in 428 cases (50 per cent), the aortic valve in 337 cases (39 per cent), the tricuspid in 68 (7.9 per cent), and the pulmonic in 24 cases (3.1 per cent). Cates and Christie, in a more recent tabulation of 408 cases, found the mitral valve involved alone in 47 per cent, the mitral and aortic valves together in 40 per cent, and the aortic valve alone in 13 per cent. They do not mention involvement of the tricuspid or pulmonic valves.

Embolic or embolic-like myocardial lesions are found in a high percentage of cases These are possibly due to emboli from the vegetations, or possibly are of an endarteritic nature. Thayer noted *acute myocarditis* in 60 per cent of his cases, but Clawson (1940) found nonspecific myocarditis in 24 per cent of the hearts Some degree of active myocarditis was found by the authors in every patient dying during the active phase of the disease.

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ment, which is a possibility following administration of streptomycin, does not seem justified in these cases.

A minority of S. viridans strains have a penicillin sensitivity of 0.2 to 1.0 unit/ml. A rare strain will *require up to 2 units/ml for in vitro destruction.* In such cases, 1 million units of penicillin administered intramuscularly every 2 to 3 hr plus 1 Gm of streptomycin (or 0.5 Gm each of streptomycin and dihydrostreptomycin) every 12 hr may be needed. In these cases, the risk of eighth nerve involvement must be taken. For the more sensitive strains of this group, injections at 3 hr intervals will probably suffice. Also, for this group, the interval between doses of penicillin can probably be lengthened to 6 hr at the end of 2 weeks and the dose of streptomycin reduced to 0.5 Gm every 12 hr. Five weeks is about the average length of treatment for the more sensitive range of this group. For organisms in the less sensitive range of this group (more than 1.0 unit per milliliter), 1 million units every 2 hr plus 1 Gm streptomycin every 12 hr must be considered. Three weeks of this plan followed by 4 weeks of the reduced regimen noted above are usually *in order.*

In the authors' earlier experience, several strains considered to be S. viridans (including two morphologically atypical strains), which required 4 to 8 units/ml for in vitro inhibition, were successfully treated with penicillin alone. In retrospect, *it is probable* that some of these organisms belonged to the enterococcus group. One was later identified as S. salivarius. If one hesitates to use streptomycin, penicillin may be tried alone in massive doses with *probenecid (Benemid).* However, if definite and satisfactory bacterial, laboratory, and clinical response does not occur by the end of a week, streptomycin should be added.

The authors have encountered great difficulty with the *regimens just outlined* because patients often object to frequent *intramuscular* injections. Also, tissue reaction to the *injections* frequently produces a slight fever and maintains *the elevation* of the sedimentation rate, thus masking two important criteria for judging the effectiveness of treatment.

Whenever the organism requires penicillin dosage of the frequency and magnitude outlined here, and particularly in enterococcic infections, the *continuous intravenous drip method* is to be preferred. One-half the total daily dose is dissolved in 500 ml of distilled water, and the number of drops per minute is adjusted to permit the 500 ml to run in in 12 hr. A fresh bottle is connected each 12 hr. Whether a needle or a polyethylene tube is used in the vein is a matter of choice. The needle need not be larger than No. 21 gage. Small amounts of heparin may be added to the penicillin solution in order to prevent local thrombosis, but this is seldom necessary. Admittedly, this method is applicable only if there is available an adequate interne or resident service or the intravenous team of a hospital. Renal blocking of penicillin excretion by probenecid (Benemid) (500 mg every 6 hr orally) approximately doubles the serum penicillin level obtainable with any given dose of penicillin by any means of administration. This may enable one to increase the intervals between injections or reduce the dose per injection in some cases.

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If clinical or bacteriologic response to the above regimens for enterococcic infections is unsatisfactory, the following scheme should be tried: oral *erythromycin* 3 Gm daily, plus 1.5 Gm *erythromycin* intravenously daily, plus *streptomycin* 2 Gm daily (or *bacitracin* to a total of 100,000 units daily). All three (*erythromycin, streptomycin,* and bacitracin) have been given simultaneously.

Although procaine penicillin G is said to be less *painful* when injected, its acceptance by *patients is not higher;* moreover, when the aqueous suspension is used, *the* serum levels obtained are *inferior.*

the sensitivity of anaerobic organisms. The authors have found most of these not to be complete anaerobes. Most of them will grow in thioglycolate broth. If this medium is used in the serial-dilution technique, not too much difficulty is encountered. If, however, the organisms will not grow satisfactorily in thioglycolate broth, evacuation of the air around the cultures and substitution of carbon dioxide may be necessary. Even in aerobic cultures, the addition of a small percentage of carbon dioxide in the surrounding atmosphere tends to enhance growth of the organisms.

Further discussion of the antibiotic sensitivity and of the antibiotic assays in relation to therapy will be found below in the section on therapy.

PATHOLOGY

The lesions found in endocarditis can be divided into those of the lining of the heart itself and those found elsewhere in the body, due to either *embolic phenomena* or a *hypersensitivity reaction.* It is also pertinent to discuss the endocardial lesions found in cases treated with penicillin (Hildebrand and Priest, 1947).

The theories as to the mode of onset of endocarditis have been described The lesions in the untreated state show essentially a necrotic core containing bacteria, over which there are successive layers of platelets and thrombi The bacteria are relatively few in number near the surface and also in the deepest portion of the lesion. Perhaps this can best be explained by the fact that, in these areas, phagocytic activity of the leucocytes is most active The area of the valve which is involved by this thrombotic process shows a chronic, and sometimes subacute, inflammatory reaction, with fibroblastic proliferation and new blood vessel formation Thus, there is not only an active inflammatory reaction present, but also a tendency toward healing The *friable* nature of the surface lesions renders them susceptible to fracture, with small pieces being broken off and forming *emboli.*

Sometimes the destructive process proceeds rather rapidly, in which instance there is more destruction of valve substance than when the inflammation is slow, as it usually is Occasionally, the process is so necrotizing that the valve is ruptured, or there is rupture of one or more chordae tendineae. A few instances of spread of the infection from the aortic valve to the adjacent sinuses of Valsalva have been reported. *Aneurysm* and *rupture of a sinus* can follow. When the process is slow, the destructive forces are in part matched by the healing forces. The protective layer of fibrin tends to protect the bacteria from leucocytes, thus enabling the former to reproduce

Moore states that healing of these lesions occurs in five general steps: (1) a covering of fibrous tissue, (2) invasion of the layer of bacteria by phagocytes, (3) calcification of the bacterial colonies, (4) hyalinization and calcification of the core of the vegetation, (5) endothelialization of the spaces and clefts in the vegetation and over the surface. This process is essentially the same as that which the authors have observed. As the healing process continues, hyalinization and excessive calcification are produced. Thus, a *valve which has healed following bacterial endocarditis is more markedly deformed than it was prior to being attacked by the bacterial infection.* This finding was outstanding in the authors' cases.

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If the organism is an enterococcus, the regimen outlined for the most resistant strains of viridens is followed. *The expected duration of treatment is a minimum of 6 weeks. A dosage requirement of 20 million units of penicillin per day is common, and as high as 100 million have been given.* Probenecid is used from the outset, and only the continuous intravenous drip method is employed. However, in a work of this kind, it would be unfair not to mention the regimen advocated by Nichols et al. as being the most satisfactory in dealing with enterococci. Here, 1,200,000 units of *aqueous procaine penicillin G* is given intramuscularly every 6 hr; 1 million units (or more) of *sodium or potassium penicillin G* in 20 to 30 ml of 5 per cent dextrose solution or saline is given intravenously three to four times daily between the intramuscular injections, probenecid and streptomycin are also used as outlined above.

If clinical or bacteriologic response to the above regimens for enterococcic infections is unsatisfactory, the following scheme should be tried: oral *erythromycin* 3 Gm daily, plus 1.5 Gm *erythromycin* intravenously daily, plus *streptomycin* 2 Gm daily (or *bacitracin* to a total of 100,000 units daily). All three (erythromycin, streptomycin, and bacitracin) have been given simultaneously.

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done on the supposition of a possible metastatic malignancy, revealed a mycotic aneurysm.

Very occasionally, a mycotic aneurysm will occur in the wall of a vessel immediately adjacent to a vein, with resultant *arteriovenous aneurysm.*

DIAGNOSIS

When the classic signs of fever, petechiae, Osler or Janeway nodes, splinter hemorrhages in the nail beds, splenomegaly, embolic phenomena, and heart murmurs are present, the diagnosis of bacterial endocarditis is obvious. However, by the time these signs appear, the disease has been present for some weeks and myocardial damage may be such as seriously to affect both the immediate and long-range prognosis *If congestive heart failure develops either before the disease is recognized or during treatment, the immediate mortality rate under the age of 45 is 33 per cent, over the age of 45, 92 per cent.*

The importance of diagnosis before the classic signs appear cannot be too strongly emphasized. This can be accomplished only by maintaining a high degree of suspicion toward those patients who are likely candidates. These include patients with known congenital cardiac lesions or acquired rheumatic valvular deformities, patients without cardiac murmurs but with a known history of rheumatic fever, patients with any cardiac murmur even though it has been considered "functional" or insignificant. Any patient in these categories who develops fever and malaise, which does not promptly and permanently subside with simple nonspecific treatment, should be suspected of having bacterial endocarditis, and proper laboratory investigation should be carried out immediately Antibiotics should not be used at this point. If they have been used for whatever reason, including rheumatic fever prophylaxis, they should be stopped until the diagnosis is established

Particular suspicion must be directed toward any *upper respiratory infection* which is followed by persistent fever and malaise beyond the natural course of the initial infection. The same holds for symptoms of *subacute illness* following tooth extraction, tonsillectomy, cystoscopy, proctoscopy, cardiac surgery or catheterization, and childbirth. Patients with dental caries or apical abscesses who develop *unexplained malaise and fever* must also be suspect.

The earliest symptoms are nonspecific. In the majority of cases, they consist of one or more of the following: malaise, aches and pains, chills, sweating, fever. Age and sex of the patient are of little help in diagnosis. No cases under age 5 have been reported. After 70 years of age, bacterial endocarditis is rare, but it is also rare for patients with congenital or acquired valvular heart disease to live past 70. The *per decade* incidence from age 11 to 69 is about the same, with a slight peak between 21 and 40. The incidence in males and females in various collections of cases ranges from 2:1 to 1:1. The comparative rarity of the disease (5 to 15 cases per 100,000 hospital admissions) makes early diagnosis the more challenging.

Once suspicion of the disease is aroused, the patient should be promptly hospitalized in an institution known to have facilities for adequate laboratory studies, as outlined in the section on bacteriology. If the hospital ordinarily used does not have such facilities, the patient should be sent elsewhere, even if out of town. Laboratory studies for infections producing similar symptoms (undulant fever, typhoid, tuberculosis, etc.) are carried out simultaneously with the investigation for possible bacterial endocarditis

A *positive blood culture* establishes the diagnosis. A *negative blood culture* does not rule out the possibility of bacterial endocarditis. If no other possible cause of the illness can be substantiated, bacterial endocarditis should be presumed and treatment started. Invasion of the endocardium by organisms of the *undulant* and *typhoid fever* groups and by *tuberculosis* does occur. In the presence of cardiac murmurs, blood cultures positive for any of these organisms must raise the suspicion of endocardial invasion, although it is possible to have such positive cultures in these diseases without the endocardium being invaded.

The foregoing applies chiefly to the *subacute form* of the disease. Diagnosis of the still much rarer *acute form* also results largely from suspicion. Here the patient is usually already hospitalized and under treatment for some acute infection such as osteomyelitis, pneumonia, puerperal sepsis, etc. Suspicion is aroused when

biotics Antibiotic-impregnated slips are placed at right angles to each other on the surface of agar plates inoculated with the organism recovered from the patient. The individual inhibitory effect of each antibiotic is indicated along the edges of the strips. The combined effect (if any) is indicated by a wider zone of inhibition at the inner angles where the strips cross

When antibiotics other than penicillin must be used, the daily dosage should be maximal or near maximal Following are suggested daily doses derived from the literature

Bactericidal Group

Bacitracin, 100,000 units

Neomycin, 500 mg intramuscularly

Polymyxin B, 2.5 mg per kilogram of body weight

Streptomycin, 2 Gm intramuscularly as synergist to penicillin or other antibiotics For susceptible gram-negative organisms, 3 to 4 Gm may be used for the first 3 to 4 days Reports differ as to the value of combining streptomycin and dihydrostreptomycin in equal parts in order to lessen toxicity

Bacteriostatic Group

Erythromycin, 3 Gm orally (base or stearate), 1.5 Gm intravenously (glucoheptonate or lactobionate). After 1 week, the oral dose is 2 Gm and the intravenous dose 1 Gm Combination of oral and intravenous administration for at least the first week is preferred by some

The *cyclines*, 4 Gm orally or 2 Gm intravenously for 3 to 7 days, then 2 Gm orally or 1 Gm intravenously

Chloramphenicol, 4 Gm orally or 2 Gm intravenously or intramuscularly for 3 to 4 days, then 3 Gm orally

Novobiocin, orally, 3 Gm for 5 to 7 days, then 2 Gm Intravenously, 2 Gm for 2 to 5 days, then 1 Gm

Endocarditis Caused by Organisms Other Than Alpha Hemolytic Streptococci or Enterococci. The most common organism encountered today is some strain of *micrococcus* (*M pyogenes* var *albus* or *aureus*). The increasing incidence of endocarditis due to these organisms is attributed in large measure to cardiac surgery. Some blame the increasing use of intravenous therapy. Endoscopic diagnostic procedures apparently account for some cases Most hospitals have been found to harbor these bacteria, which are generally highly resistant to penicillin The chances of effecting a cure are 50 per cent or less. If the recovered organism is sensitive to 1 unit/ml or less of penicillin, it alone in daily dosage not less than 10 million units may be effective The necessity to give injections every 2 or 3 hr makes administration by continuous intravenous drip preferable. *Probenecid*, 500 mg orally, is given every 6 hr

For any strain requiring more than 1 unit/ml of penicillin for in vitro inhibition, one of the following combinations should be used· *penicillin and streptomycin; penicillin, streptomycin, and erythromycin; penicillin, streptomycin, erythromycin, and oxytetracycline* These combinations resulted in cures in six out of seven cases (Melton and Logue) Daily penicillin dosage in these cases ranged from 50 to 12 million units Combinations not including penicillin have been used as follows (Finland). *erythromycin plus bacitracin, streptomycin, chloramphenicol, or one of the tetracyclines*, the same combinations but using *novobiocin* in place of erythromycin, or *bacitracin plus chloramphenicol or streptomycin* It is understood that the offending organism must be at least moderately sensitive to any antibiotic chosen Maximum tolerated doses administered parenterally for the first week are necessary. Oral administration and reduction in dosage must not take place until fever and bacteremia have subsided. If such response is not obtained by the end of the first week, some other combination should be used. Regardless of the sensitivity of the micrococcus in question, treatment must be continued for at least 6 weeks.

Endocarditis Caused by Other Organisms. Combinations of antibiotics are most frequently used here The following suggestions are taken from the literature, much of which deals with individual case reports The infecting organism is usually highly or completely resistant to penicillin. In such cases, penicillin, even in huge doses, had best be abandoned, and a combination of antibiotics giving the most promise by sensitivity tests should be used Sometimes, the addition of an antibiotic of only moderate promise in the laboratory may help turn the tide where more apparently effective antibiotics had been failing. The difference between bactericidal and bacteriostatic agents is less important here. However, if they have an equal effect on the organism in vitro, the bactericidal agents should be selected initially Maximum dosage must be given from the outset, parenterally whenever the agent can be administered in this manner. The minimum duration of treatment is 6 weeks Much longer is commonly necessary. Some authors

varies in different individuals. Also, organisms of the same sensitivity in vitro will not be eradicated by the same serum concentration in vivo. Probably, the percentage loss in penicillin concentration during diffusion through the fibrin barrier varies. The authors most recent patient had an organism with a sensitivity in vitro of 0.01 units per milliliter. Yet a serum level of penicillin which was never less than 1.6 units per milliliter was inadequate for cure. A serum level of 3 to 6 units per milliliter (300 to 600 times the in vitro sensitivity) was necessary. With organisms of this low resistance, many cures with serum levels of less than 1 0 unit per milliliter were obtained: these were the early cures with a daily dosage of 250,000 to 400,000 units.

A minimum of 4 weeks treatment was dictated by early experience as being necessary for cure. In general this remains true, except in selected cases, as will be discussed later When *depot or long-acting penicillin preparations* became available, it was learned that the frequency of injections ordinarily adequate was not valid for bacterial endocarditis Regardless of the preparation used, the serum concentration of penicillin resulting from a single dose reaches a peak, either abruptly or slowly, depending on the type Then, the concentration declines steadily, the rate depending on the type of penicillin and the patient's rate of excretion In treating bacterial endocarditis, it is imperative that the next dose be given before the curve of declining serum concentration falls below the optimum for killing the organism in question. Understanding of these basic principles is a prerequisite to the successful treatment of bacterial endocarditis

Modern Concepts. In addition to blood cultures according to the method described in the section on bacteriology and tests relating to other infectious diseases, the following additional minimal laboratory work should be done. complete blood count, urinalysis, sedimentation rate, Kahn test, 2-meter PA and left lateral x-rays of the chest, electrocardiogram Other laboratory tests may be dictated by features of the individual case or the routine of the attending physician.

While waiting for reports on the blood cultures and other laboratory tests, penicillin therapy should be started. Until the identity and antibiotic sensitivity of the organism are known, dosage is empirical Penicillin is selected initially because 87 per cent of organisms encountered are sensitive to it within therapeutic range. *Potassium penicillin G,* 1 million units, is given intramuscularly every 6 hr around the clock. Varying the site of injection is important for the patient's comfort. The arms should not be used. On the second or third day, blood should be drawn just before a dose of penicillin is given and the serum penicillin level determined.

When the identity of the organism and its antibiotic sensitivity are known, therapy is adapted to the individual patient.

Since 1945 a voluminous literature concerning therapy of bacterial endocarditis has accumulated. While the basic principles remain unaltered, some modifications of and additions to therapy should be understood as treatment is being planned for a specific patient. Finland has written an excellent review. It must be remembered that suggested dosage for the sensitivity range of a given organism represents a generalization. The actual dosage for a specific patient must ultimately be determined by the individual clinical response

If the organism is a streptococcus, it will usually be either the *S. viridans* or an *enterococcus* (including *S. salivarius*). If it is *S. viridans* and sensitive to 0 1 unit/ml or less of penicillin (and a large majority are), the initial dose of 1 million units every 6 hr may be reduced to 500,000 or 600,000 units every 6 hr. Successful treatment of viridans endocarditis where the organism was sensitive to 0.1 unit/ml or less of penicillin has been accomplished in 2 weeks (Hunter and Paterson) with daily doses of 2 to 12 million units of penicillin plus 1 to 2 Gm of streptomycin daily. One would be tempted to plan only a 2 weeks course of treatment for such a patient.

Tompsett et al. secured 24 definite and 8 probable *bacteriologic* cures by this method in a series of 35 patients with viridans endocarditis whose [illegible]

short as 14 days falls short of the goal of antimicrobial therapy, which is bacteriologic cure in all cases." Jawetz agrees that any course of treatment of less than 3 weeks duration is unreliable, and the authors concur in this opinion.

Certainly, a physician, whose experience in treatment of this disease is limited to the occasional case seen in private practice, should not plan on a 2 weeks course. The necessity of adding streptomycin (or dihydrostreptomycin) in treating organisms having a penicillin sensitivity of 0 1 unit/ml or less can be questioned. Since penicillin has been in abundant supply, the authors had no failures with penicillin alone in organisms of this group sensitivity. The risk of eighth nerve involve-

resumed. If all criteria (normal temperature, clinical improvement, absence of peripheral phenomena, sterile blood cultures, absence of splenomegaly, behavior of sedimentation rate, and leucocyte count) remain satisfactory for a week, treatment is discontinued, the patient is discharged from the hospital (if his general condition is satisfactory), and the immediate follow-up period begins.

Follow-Up. For the first four weeks, the patient takes and records his temperature four times daily. Twice weekly, observations of the clinical condition, sedimentation rate, leucocyte count, and blood cultures are made. Activity is geared to the clinical evidence of myocardial damage. The majority of patients should remain at home at a relatively inactive level. If temperature and laboratory data continue normal for 2 weeks after leaving the hospital, the interval between observations may be lengthened to once a week, and blood cultures discontinued. Other observations as above should be continued. At the end of 2 months, the interval between observations may be increased to 2 weeks. By this time, most patients will have returned to work, if of a sedentary nature. By the end of the fourth month after apparent arrest of the active phase, the interval between observation may be lengthened in most cases, but should not be discontinued until 6 months have elapsed.

A steadily rising sedimentation rate, with or without fever or leucocytosis, means *reactivation of a suppressed, but not cured, infection.* There has been no exception to this in the authors' experience, and the steadily rising sedimentation rate has preceded positive blood cultures and other definitive findings by as much as 3 weeks. Such reactivation may not take place for 4 months (some observers claim 6 months). Since it can be assumed that the same organism is present, a fresh course of treatment, using the previously effective antibiotic, may be started without waiting for blood cultures to become positive. If clinical response is not prompt, treatment should be stopped and an attempt made to isolate the infective organism by means of the previously described blood-culture techniques.

PROGNOSIS

Immediate. Recovery from the active phase of the disease depends upon (1) the severity of preexisting myocardial damage; (2) the severity of the acute myocarditis produced by the active phase of the disease; (3) the extent of damage to other organs, chiefly the result of embolism; occasionally fatal intestinal hemorrhages occur, more rarely a fibrinous pericarditis; (4) the sensitivity of the organism to a bactericidal antibiotic, (5) the absence of allergy to the necessary antibiotic.

If the organism is reasonably sensitive, and unless the patient is virtually moribund when first seen, the duration of the disease prior to therapy does not significantly alter the chances for arrest of the active phase. However, it does increase the chance of fatal or severely crippling embolism.

Patients with previous clinical evidence of severe myocardial damage and history of repeated congestive heart failure may die of congestive failure during the active phase of bacterial endocarditis. Death is due to the associated acute myocardial involvement, not to the valvular lesion. With these exceptions, there is no excuse for failure to arrest a case of *S. viridans* endocarditis of up to moderate sensitivity of the organism to penicillin. If the bacterial invasion includes the chordae tendineae of the mitral valve, calcification incident to healing or necrosis may result in *rupture of the chordae,* with sudden production of severe and rapidly fatal *mitral regurgitation,* even though the valvular endocardial process is completely healed. The authors have observed one such occurrence just as the patient was ready to be discharged from the hospital. Autopsy revealed the above findings.

When dealing with a markedly resistant strain of streptococci or other organism, the immediate prognosis is always grave. The chance of a successful outcome is rarely more than 50 per cent.

Long Range. A continuing study of the 21 survivors from the original group of 44 (Priest and Smith, 1943) revealed the following data:

Only 2 of these patients had symptoms of impaired cardiac function prior to endocarditis, although 10 had varying degrees of cardiac enlargement by x-ray and 3 of them had specific electrocardiographic abnormalities. During the first 9 years 5 patients died, but only 1 as the result of residuals of bacterial endocarditis. This patient developed chronic glomerulo- and pyelonephritis and hypertension. His death in the seventh year

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Since 1945 a voluminous literature concerning therapy of bacterial endocarditis has accumulated. While the basic principles remain unaltered, some modifications of and additions to therapy should be understood as treatment is being planned for a specific patient. Finland has written an excellent review. It must be remembered that suggested dosage for the sensitivity range of a given organism represents a generalization. The actual dosage for a specific patient must ultimately be determined by the individual clinical response.

If the organism is a streptococcus, it will usually be either the *S. viridans* or an *enterococcus* (including *S. salivarius*). If it is *S. viridans* and sensitive to 0.1 unit/ml or less of penicillin (and a large majority are), the initial dose of 1 million units every 6 hr may be reduced to 500,000 or 600,000 units every 6 hr. Successful treatment of viridans endocarditis where the organism was sensitive to 0.1 unit/ml or less of penicillin has been accomplished in 2 weeks (Hunter and Paterson) with daily doses of 2 to 12 million units of penicillin plus 1 to 2 Gm of streptomycin daily. One would be tempted to plan only a 2 weeks course of treatment for such a patient.

Tompsett et al. secured 24 definite and 8 probable *bacteriologic* cures by this method in a series of 35 patients with viridans endocarditis whose organism sensitivities ranged from 0.002 to 0.1 unit/ml in 26 of these patients They conclude that "the use of this (combined) therapy for a period as short as 14 days falls short of the goal of antimicrobial therapy, which is bacteriologic cure in all cases." Jawetz agrees that any course of treatment of less than 3 weeks duration is unreliable, and the authors concur in this opinion

Certainly, a physician, whose experience in treatment of this disease is limited to the occasional case seen in private practice, should not plan on a 2 weeks course The necessity of adding streptomycin (or dihydrostreptomycin) in treating organisms having a penicillin sensitivity of 0.1 unit/ml or less can be questioned. Since penicillin has been in abundant supply, the authors had no failures with penicillin alone in organisms of this group sensitivity The risk of eighth nerve involve-

2

Pathology of pericarditis and constrictive pericarditis

IRA GORE

ACUTE AND SUBACUTE PERICARDITIS

Inflammation is the commonest affliction of the pericardium. Smith and Willius found evidence of it in 4 2 per cent of 8,912 necropsies at the Mayo Clinic prior to 1932, more than half the cases were acute Moreover, there has been no lessening of its frequency since the advent of effective chemotherapy Griffith and Wallace reported an incidence of 5 4 per cent in a large autopsy series covering the period 1940 to 1946 Approximately one-third of adult autopsies and two-thirds of those showing chronic valvular disease present ovoid milky thickenings and opacities of the visceral pericardium If these superficial acellular fibroses were to be included in any tabulation of pericarditis, its incidence would be far higher than any reported

The etiologic factors may be *infectious* or *noninfectious* The former includes direct *bacterial involvement*, such as pneumococcal, streptococcal, staphylococcal, or tuberculous infection, rare *fungal infections, nonbacterial forms*, such as rheumatic fever and acute benign pericarditis, and *parasitic infections*, such as amebiasis, trypanosomiasis, trichinosis, cysticercosis, and echinococcosis

Organisms reach the pericardium from lesions of the myocardium, by the blood stream, or by direct or lymphatic extension from neighboring mediastinal or pleural disease The great majority of *purulent pericarditis* is secondary to septic processes within the thorax *Noninfectious* causes of pericarditis include myocardial infarction, uremia, neoplasm, trauma, and such idiopathic diseases as disseminated lupus erythematosus, scleroderma, and *periarteritis nodosa*

Pathologically, *acute* and *chronic* forms of inflammation occur. In the former, fine meshlike deposits of *fibrin*, first in the region of the great vessels, roughen and thicken the normally smooth translucent serous membrane Deposition may be so extensive that it covers the entire serosal surface. Irregularities in its thickness result from the rhythmic action of the heart *Serous effusion* of variable degree accompanies the fibrinous inflammation. Where it is minimal, the term *pericarditis sicca (dry pericarditis)* is applicable, at times, the volume of the effusion may overshadow other evidences of inflammation.

An admixture of large numbers of granulocytes, many degenerating, characterizes *suppurative or purulent pericarditis*. Frankly bloody exudate justifies the term *hemorrhagic pericarditis*, but this should not be confused with intrapericardial hemorrhage or *hemopericardium* For practical purposes, large effusions should be considered of inflammatory origin, though a very small percentage are due to congestive failure or myxedema. The normal pericardial fluid volume ranges from 10 to 60 ml, but effusions of less than 300 ml are usually not apparent clinically.

It is impossible to determine the etiology of a given case of pericarditis from its gross ap-

Benzathine penicillin G (Bicillin) should *not* be used.

Endocarditis due to very sensitive streptococci has been successfully treated by oral administration of *phenoxymethyl penicillin (V-Cillin)* (Santos-Buch et al.). This method is not advisable unless one has considerable experience in the treatment of bacterial endocarditis.

Individual *allergy* to penicillin appears to be on the increase, judging by statements made by patients. Such statements should not deter the physician from trying to use penicillin in the treatment of bacterial endocarditis. Skin testing for sensitivity should be done. An initial daily dosage of 1 million units of penicillin plus streptomycin and *antihistaminics* may be tried at the outset. If minimum serum levels of penicillin obtained with this dosage fail to meet the requirements outlined above, and the patient is showing no allergic reaction, the daily dosage may be gradually increased

One patient started and maintained on 10 million units per day (an excessive dose considering the sensitivity of the organism) developed a generalized rash erroneously thought to be petechiae. Stopping penicillin for a few days, plus use of antihistaminics, resulted in disappearance of the rash Resumption of penicillin at the rate of 2 million units a day gave adequate serum levels and resulted in cure without recurrence of the rash

There will be the occasional patient whose sensitiveness to penicillin is so marked that no amount can be given without danger of severe *exfoliative dermatitis*. In such cases, recourse must be had to other antibiotics of the bactericidal group (see below) to which the organism in question is most sensitive. In these cases, the chance for cure is significantly reduced *Cortisone* or *ACTH* should *not* be used, except for short periods in the effort to combat allergic reaction to penicillin

Antibiotics Other Than Penicillin. None of these antibiotics should be thought of unless the organism in question is wholly resistant to penicillin or so highly resistant that securing an adequate serum level would require impractical or impossible daily dosage, or unless the patient is so sensitive to penicillin that it is not safe to use it.

BACTERIOSTATIC AGENTS. Erythromycin (also Erythrocyn, Ilotycin), chloramphenicol (Chloromycetin), tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn), chlortetracycline (Aureomycin), oxytetracycline (Terramycin), and novobiocin belong to this group Other erythromycin-like agents are carbomycin, oleandomycin, and spiramycin. These should never be used alone, no matter how sensitive to them the organism is in vitro Blood stream sterilization and temporary clinical improvement may be obtained, but relapses are almost certain to occur, and the organism will then be found to be resistant. This is particularly true of gram-positive organisms. Some gram-negative organisms may respond to one of these alone. But even here, it is better to combine one of these antibiotics with streptomycin or polymyxin B. The combination of one of them with bactericidal antibiotics has been of value in some micrococcic infections.

BACTERICIDAL AGENTS. Bacitracin, neomycin (also Mycifradin), and polymyxin B (also Aerosporin) belong to this group. Because of the danger of producing irreversible deafness and transitory kidney damage, neomycin should be used only in desperate situations, and then for not longer than 2 weeks.

In testing for organism sensitivity, only one representative of a group need be used, e g, the various cyclines and mycins In combining antibiotics, it is useless to use more than one analogue of a group.

It has been said that bacteriostatic antibiotics tend to antagonize the effect of the bactericidal group in vitro (Jawetz and Gunnison). The highest degree of antagonism is reached when penicillin and chloramphenicol are used However, Eleck and Hilson found that, by longer incubation, the antagonistic effect of these substances may be replaced by synergism. They suggest that this is what may take place in vivo to explain the reported cures when supposedly antagonistic antibiotics were used. Judged by their studies, the following combinations were most frequently synergistic when used against organisms recovered from cases of bacterial endocarditis: penicillin and streptomycin, streptomycin and bacitracin, streptomycin and chloramphenicol. They conclude that, when penicillin in dosages to attain 25 units/ml of serum concentration, plus streptomycin or bacitracin, is not effective, one of the bacteriostatic agents plus streptomycin is justified

Pilkington et al. suggest a simple method for determining the synergistic action of pairs of anti-

processes elsewhere, is composed of nodular aggregates of epithelioid cells, *caseous necrosis*, and a variable quantity of newly formed fibrous tissue Although the effusion which characterizes the acute stage diminishes over a period of several months, it is the long persistence of poorly resorbed caseous material which stimulates progressive scarring. Unfortunately, this process, which circumscribes and delimits the infection, is the very one which so frequently results in cardiac constriction. The development of this complication was observed in 11 of 41 cases of acute tuberculous pericarditis (Bauer et al) Although streptomycin, para-amino salicylic acid, and isoniazid have greatly improved the once gloomy prognosis of the acute disease, it is noteworthy that 8 of the 11 cases of constrictive pericarditis had developed despite chemotherapy

The frequency of *metastatic neoplastic involvement of the pericardium* is not generally appreciated since there are often no clinical symptoms to suggest it Pericardial effusion of variable degree is the usual manifestation, it accumulates slowly so that tamponade rarely occurs Variable quantities of blood and fibrin accompany the effusion, but diagnostic significance can be attached only to the recognition of *tumor cells* in the sediment As illustrated in Table 8-1, somewhat more than one-fourth of patients with breast and lung carcinoma develop pericardial metastases These tumors, it will be recalled, frequently involve the mediastinal nodes, which also drain the pericardial lymphatics Young and Goldman found mediastinal metastasis in more than 70 per cent of their 91 cases of secondary cardiac tumors comprising 19 per cent of 476 malignancies, almost twice the frequency reported by Goudie The blood stream is the usual route of metastasis in melanoma, leukemia, sarcoma, and an appreciable proportion of carcinoma. About two-thirds of pericardial metastases simultaneously involve the myocardium

Primary *tumors of the pericardium* are even more rare than those of the heart Two cases of pericardial leiomyoma have been reported Other benign mesenchymal tumors which total only 39 in 1945 include lipoma, fibroma, angioma, and neurofibroma Intrapericardial teratomas, 5 of which were reported in infants or young children up to 1946, are merely positional variants of the more common mediastinal lesion Malignant pericardial growths are at least

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pattern, papillary glandlike epithelial growths are intimately interspersed with sarcomatous stromal growth. Wide quantitative variation of the two cell types accounts for difficulty in the proper identification of individual tumors.

Clinically benign or malignant pericardial lesions may be manifest as pericarditis with fever, pain, and friction rub. Often, indeed, there may be a deceptive remission which blunts the alertness of the clinician Radiologically, the recognition of a bizarre cardiac silhouette is of diagnostic value. Cardiologists, too, find bizarre ECG changes which seem related to variable interference with rotation of the heart during systole and diastole. Correlation of these findings with the clinical absence of other heart disease should provide the physician with a high index of suspicion, especially if the patient is known to harbor a malignant tumor elsewhere Under these circumstances, too, there is often myocardial in-

TABLE 8-1. SECONDARY TUMORS OF THE PERICARDIUM AND HEART

Tumor type	*Total*	*Pericardial involvement*	
		No.	*Per cent*
Reticulum-cell sarcoma	9	6	67
Lymphocytic leukemia	11	6	55
Melanoma	10	5	50
Breast carcinoma	45	16	32
Lung carcinoma	115	41	27
Granulocytic leukemia	14	2	14
Renal carcinoma	33	4	12
Rectal carcinoma	39	4	10
Pancreatic carcinoma	45	4	9
Esophageal carcinoma	13	1	8
Lymphosarcoma	61	4	7
Ovarian carcinoma	19	1	5
Hodgkin's	22	1	5
Uterine cervical carcinoma	49	2	4
Urinary bladder carcinoma	25	1	4
Prostatic carcinoma	56	2	4
Gastric carcinoma	201	2	1

SOURCE From Scott and Garvin

have continued one or more of the effective agents in an average dosage for one or more months after apparent cure. The cure rate is distressingly low.

Brucella Endocarditis. Tetracycline or streptomycin. Aortic valve most commonly affected.

Aerobacter Group. Streptomycin or polymyxin B plus tetracycline or chloramphenicol.

Pseudomonas aeruginosa. Polymyxin B (most effective) plus streptomycin.

Proteus Group. Streptomycin plus tetracycline or chloramphenicol. Polymyxin B is not effective.

Salmonella Group. Chloramphenicol. Chloramphenicol plus polymyxin B. Tetracyclines, alone or with polymyxin B. Combination of all three. Results are most disappointing regardless of therapy. Spontaneous cures have been reported.

Hemolytic Streptococci (Other Than Viridans); Pneumococcus. Penicillin in daily dosage of 2 to 3 million units

Gonococcus. Very rare. Aortic and pulmonic valves are most likely to be involved. Long-range prognosis is poor because of severe aortic or pulmonic regurgitation (Olson and Fabricus). Penicillin in daily dosage of 2 to 3 million units.

Meningococcus. Penicillin, 12 million units per day divided in 12 doses or by continuous intravenous drip to start, plus full doses of sulfadiazine The latter addition is suggested by Kellow and Dowling because of the marked sensitivity of the meningococcus to sulfa Although apparently unable to penetrate fibrin by themselves, the sulfa drugs are seemingly carried by penicillin through the fibrin barrier (Priest and McGee).

Influenzae Group. Streptomycin in full doses

Erysipalothrix rhusiopathiae. Penicillin, 12 million units or more per day plus streptomycin.

Yeasts and Molds. Of the reported cases diagnosed clinically, none recovered regardless of various combinations of therapy Mycostatin is not effective

Herrellea vaginicola Combination of erythromycin, streptomycin, oxytetracycline, and sulfadiazine

General Measures. Absolute *bed rest* is indicated until the patient is afebrile and the heart rate has returned to normal If congestive failure is present at the outset of or develops during treatment, bed rest must be prolonged until compensation has been restored *Activity* should not exceed the "armchair" level with bathroom privileges until the active phase of the infection is definitely arrested *Diet* should be high in calories, vitamins, and proteins. Unless congestive failure is present, sodium should not be restricted below 4 Gm per day. If *anemia* is marked, intravenous administration of *packed red cells* is more effective than ferrous salts by mouth. A good *multiple-vitamin* preparation is desirable. *Digitalis* and *mercurial diuretics* are not indicated, except in the presence of congestive failure. Removal or other appropriate treatment of any discoverable *foci* of infection is indicated. If clinical evidence of infection persists, in spite of adequate dosage of appropriate antibiotics over many weeks, splenectomy may be considered (Lingeman et al.).

Criteria for Success of Therapy. Obviously, a positive blood culture indicates inadequate dosage or incorrect selection of antibiotic (or combination of antibiotics) or an organism resistant to any therapy. Once treatment is started, negative blood cultures are meaningless. *The blood stream may be kept sterile with dosages totally inadequate for cure of the endocardial infection.* Likewise, normal temperatures and apparent clinical improvement are no assurance that the endocardial process is being successfully attacked. In the experience of one of the authors (Priest and McGee), the only completely reliable indication of adequate therapy is a steadily declining sedimentation rate plus a steady lowering of the leucocyte count (in case the latter has been elevated).

Arrest of the active phase of the disease cannot be considered to have occurred until the sedimentation rate and leucocyte count have returned to normal and remained there for at least a week. Local tissue reaction to large doses of penicillin, given intramuscularly, may keep the sedimentation rate, and sometimes the leucocyte count, slightly to moderately above normal, after declining from the initial levels At this point, the values remain relatively constant Similar behavior may be observed, but less frequently, when penicillin is administered by continuous intravenous drip. It is assumed that coincidental foci of infection capable of causing elevation of the sedimentation rate or leucocyte count have been eradicated. After a week or so of such slightly increased values, therapy may be interrupted in order to determine if local tissue reaction is the factor.

Leucocyte counts and sedimentation rate evaluations must be made every other day. A progressive rise indicates that the bacterial process is not arrested, and therapy must be

processes elsewhere, is composed of nodular aggregates of epithelioid cells, *caseous necrosis*, and a variable quantity of newly formed fibrous tissue. Although the effusion which characterizes the acute stage diminishes over a period of several months, it is *the long persistence* of poorly resorbed caseous material which stimulates progressive scarring. Unfortunately, this process, which circumscribes and delimits the infection, is the very one which so frequently results in cardiac constriction. The development of this complication was observed in 11 of 41 cases of acute tuberculous pericarditis (Bauer et al.). Although streptomycin, para-amino salicylic acid, and isoniazid have greatly improved the once gloomy prognosis of the acute disease, *it is noteworthy* that 8 of the 11 cases of constrictive pericarditis had developed despite chemotherapy

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Primary *tumors of the pericardium* are even more rare than those of the heart Two cases of pericardial leiomyoma have been reported Other benign mesenchymal tumors which total only 39 in 1945 include lipoma, fibroma, angioma, and neurofibroma Intrapericardial teratomas, 5 of which were reported in infants or young children up to 1946, are merely positional variants of the more common mediastinal lesion. Malignant pericardial growths are at least as frequent as the benign forms. More than half of the 45 compiled by Mahaim were considered mesothelial. Histologically, mesothelial growths exhibit a biphasic cellular pattern, papillary glandlike epithelial growths are intimately interspersed with sarcomatous stromal growth. Wide quantitative variation of the two cell types accounts for difficulty in the proper identification of individual tumors.

Clinically benign or malignant pericardial lesions may be manifest as pericarditis with fever, pain, and friction rub. Often, indeed, there may be a deceptive remission which blunts the alertness of the clinician. Radiologically, the recognition of a bizarre cardiac silhouette is of diagnostic value. Cardiologists, too, find bizarre ECG changes which seem related to variable interference with rotation of the heart during systole and diastole Correlation of these findings with the clinical absence of other heart disease should provide the physician with a high index of suspicion, especially if the patient is known to harbor a malignant tumor elsewhere. Under these circumstances, too, there is often myocardial in-

was due to *occlusion of the left main coronary artery* by a calcific embolus from the healed mitral valve. The remaining 4 patients died in the fourth, eighth, and ninth years, of noncardiac related diseases. All had been actively engaged in gainful occupations, with few or no cardiac symptoms up to the time of death. One patient known to have Marfan's syndrome, died in the eleventh year after 2 years of a progressive downhill course due to the latter disease.

The present approximate 15-year status of the remaining 15 is as follows: Eleven are asymptomatic at unrestricted levels of activity. Two are moderately restricted as to activity but still economically useful and have had no episodes of congestive failure. Two would be classed as chronic cardiac invalids. Both have marked cardiomegaly, have had more than one attack of acute congestive failure, and have required digitalis and diuretics. One is still able to perform the lighter forms of housework, while the other has worked steadily at a sedentary job.

Patients treated since this original group have followed the same general pattern.

Data from this study suggest the following conclusions. (1) Bacterial endocarditis does not have a gloomy long-range prognosis, in so far as cardiac disability is concerned. (2) The ultimate fate of the large majority of patients is determined, not by the residuals of the endocardial involvement, but by the severity or nature of the preexisting myocardial damage or cardiac anomaly, and the subsequent presence or absence of rheumatic activity, coronary artery disease, and hypertension, or the rare occurrence of chronic glomerulo- or pyelonephritis (3) Severity of the myocarditis incident to the active phase of bacterial endocarditis plays a greater part in determining future cardiac impairment than residual valvular damage. (4) Duration of the bacterial process prior to therapy does not seem to influence the long-range prognosis, once the patient recovers from the active phase of the disease.

PROPHYLAXIS

When patients with known rheumatic cardiac valvular deformities or congenital cardiac lesions or who have had bacterial endocarditis require dental procedures, diagnostic instrumentation of the lower bowel or bladder, cardiac surgery, cardiac catheterization, or surgery of the upper respiratory or urinary tract, it is the custom to administer antibiotics in the hope of combating transient bacteremia resulting from these procedures and thus preventing the invasion of a previously damaged endocardium. According to Finland and others, the efficacy of such prophylaxis is not proved Nevertheless, the following measures are advised. injection of 400,000 units of procaine penicillin G and 200,000 units of aqueous crystalline penicillin G 1 hr before the contemplated procedure. This is repeated daily for at least each of the three successive days. If the contemplated procedure involves the intestinal or urinary tract, 2 million units of penicillin and 1 Gm of streptomycin daily are preferred. Since these measures may fail, the patients in question must be carefully followed for several weeks after the procedures. Following cardiac surgery, penicillin and streptomycin should be given for a week, or longer, if there is fever.

dium, are more delicate, more cellular, and more vascular; hyaline fibrosis and calcification are infrequent On the *epicardial* side, involvement is invariably superficial to the fat; the parietal pericardium, denser than the adhesive bands, maintains its integrity.

Not only the character of the constricting adhesions but their position and extent determine the characteristic hemodynamic disorder *Catherization studies* in man and in animals have shown the importance of constriction of both ventricles, particularly the left, in producing a low cardiac output incapable of increasing adequately with exercise Restriction of diastolic expansion accounts for elevation of systemic and pulmonary *venous pressures.* Pulmonary congestion is present regularly, but a lowered capacity of the right ventricle accounts for the infrequency of *pulmonary edema and paroxysmal* dyspnea, contrary to the situation in mitral stenosis

Constriction of the venae cavae or of the right atrium may be found occasionally, but as an isolated condition it does not seem capable of producing the syndrome of chronic pericardial constriction.

Two other situations, diffuse *myocardial fibrosis* and *endocardial sclerosis*, may mimic the circulatory disorder of constrictive pericarditis, since in each, the distensibility characteristics of a fibrous sac is substituted for that of normal ventricular muscle. Although there is neither an etiologic nor a pathologic relationship, it has become apparent that *myocardial weakness contributes to the hemodynamic* disturbance in individual cases of constrictive pericarditis It also presumably accounts *for the frequency of such* atypical features as *cardiac enlargement* (in about half the cases) and *normal fluoroscopic heart action (in about one-fifth of cases)*. The therapeutic and prognostic implications of such complication are obvious.

Constrictive pericarditis is an uncommon condition Between 1930 and 1954, there were only 25 instances of it at the Presbyterian Hospital in New York City, during the same period, a clinical diagnosis of *pericarditis* had been established 416 times Armstrong found a virtually identical frequency, 6 instances among 114 cases of adherent pericardium The combined cumulative experience of the Massachusetts General Hospital and of P. D. White (between 1911 and 1918) totaled 53 cases. It is perhaps the special interest of this group which accounts for the sharp increase to 78 cases by 1956. The disorder is commoner *among males than females* in the approximate proportion of 8·3. Except for infancy all ages seem vulnerable; reported cases range from 2 to 78 years. *On the* basis of increased experience, an earlier impression that it predominated in the young has been revised; about half the cases have their onset after the age of 10 years

Most Common Causes. Despite the availability of histologic sections, the *etiology* of constrictive pericarditis is obscure. The acute and *subacute phases*, which necessarily precede pericardial scarring, are often subclinical. Considering the various known causes of acute pericarditis, Andrews, Pickering, and Sellors concluded that only tuberculosis could produce cardiac constriction. Its development was observed in 16 of 18 cases of acute tuberculous *pericarditis, either isolated or part of a* multiple serosal cavity infection (polyserositis) Isolation of tubercle bacilli from pericardial fluid *is not easily accomplished;* moreover, with chronicity there is replacement of histologically (and bacteriologically) identifiable tuberculous tissue by nonspecific dense fibrous tissue *Accordingly, the true incidence* of an acid-fast etiology is virtually impossible to ascertain. Though, in different studies, the *proportion of cases regarded as tuberculous* varies considerably, it is uniformly accepted as *a* cause, if not *the* cause, of constrictive pericarditis.

Indeed, the statement has been made that, whenever the etiology is apparent, it is invariably tuberculous White and Churchill established a *tuberculous etiology* in 5 of 37 cases, Blalock and Burwell found 21 tuberculous cases among 28, Harrington, 5 of 24 cases, Sellors, 16 of 20, Paul et al, 9 of 53, Holman, 4 of 9; McKusick, 8 of 20, and Deterling and Humphreys, 8 of 25

More extensive experience with pericarditis reveals other, nontuberculous, etiologies for the *constrictive syndrome. Trauma* as a proximate cause has been well documented in 4 of the 25 cases reported by Deterling and *Humphreys.* With a dwindling incidence of tuberculosis and an increasing *number of high-speed accidents*, moreover, trauma may prove *to have* growing importance. *Rheumatic fever* is an exceedingly rare cause, but one of Deter-

pearance. To this end, proper consideration must be given to the state of the myocardium and endocardium, to the presence of systemic infection, and to the status of renal function. Preble (1901) found that acute pericarditis (244 cases) was due to pneumonia in 34 per cent, rheumatic fever in 28.4 per cent, uremia in 11 per cent, tuberculosis in 10 per cent, sepsis in 4.7 per cent, aneurysm (probably including myocardial infarction) in 2.6 per cent, typhoid fever in 1.7 per cent, and other causes in 7.6 per cent of cases. Better control of bacterial infectious processes is reflected by Griffith and Wallace's recent analysis in which *nonspecific idiopathic pericarditis* was most frequent. Pathologic findings, of course, do not reflect the frequent occurrence of acute benign pericarditis, a self-limited process, often with coexistent pleuritis, possibly viral in origin, which may mimic coronary occlusion or acute abdominal disease. *Uremia* and *myocardial infarction* generally produce a sterile fibrinous reaction without significant effusion.

Rarely *acute rheumatic carditis* may be the cause of a hemorrhagic effusion; more commonly, the reaction is predominantly fibrinous. Microscopically, foci of fibrinoid necrosis and nodular infiltrates, analogues of Aschoff bodies, may be found in the epicardium in addition to the nonspecific organizing inflammatory reaction beneath the fibrin deposits. The process may also extend into and involve the contiguous mediastinum and accounts for the development of infrequent cases of *adhesive mediastinopericarditis*, in which dense fibrous adhesions bind the heart and its adherent pericardium to the anterior chest wall and lungs. The cardiac embarrassment which accompanies this condition is attributable to the chronic valvular disease which is invariably present and must be distinguished from constrictive pericarditis.

Acute nonspecific pericarditis is synonymous with *acute benign or acute idiopathic pericarditis;* less frequent terms are acute relapsing, fugitive, or cryptic pericarditis. As the name implies, it is a process which runs a brief course and has a uniformly favorable prognosis, though there may be one or more relapses. Males are affected more than three times as often as females; though no age group is exempt, it is more often observed in the second to fourth decades. Virtually all patients have chest pain aggravated by breathing and movement, chills and fever, mild leucocytosis of variable duration, and an elevated sedimentation rate. In most cases, there is a history of an antecedent upper respiratory infection and there are coexistent signs of pulmonary or pleural disease. In 60 to 75 per cent of cases, a *pericardial friction rub* may be heard at some time during the course of the illness. An effusion is detectable in somewhat more than a third of cases. Duration of illness varies from 2 weeks to 3 months. Relapse is a frequent occurrence and took place in about one-third of Scherl's cases. Electrocardiograms are of considerable diagnostic value and, with the determination of serum transaminase levels, should help in distinguishing the condition from myocardial infarction. Assessment of treatment is difficult because all patients recover without sequelae.

Tuberculous pericarditis, always secondary to an extrinsic focus, usually in the mediastinum or pleura, produces a massive effusion up to 3,500 ml, which at times may be hemorrhagic or fibrinous. According to Spidick, 7 per cent of acute pericarditis is tuberculous and is found in 2.5 to 7.8 per cent of tubercular autopsies. The disease is three to four times more frequent in males and affects all age groups. The greater frequency among Negroes reflects only the higher prevalence of pulmonary tuberculosis. The acute phase may be relatively symptomless, and difficulties arise only with chronicity and the development of constrictive pericarditis. In the absence of tamponade, constitutional symptoms of an effusion are slight. Cardiac embarrassment is related more to the rapidity of accumulation than its size, fluid reaccumulates rapidly after a tap. The fluid is invariably *hemorrhagic,* with a predominance of lymphocytic and mononuclear inflammatory cells. The protein content is usually high, but Andrews et al. did not find that this feature distinguished inflammatory and noninflammatory effusions. Acid-fast organisms are difficult to demonstrate, and definitive diagnosis generally requires culture or animal inoculation. *Pneumopericardium* and x-ray examination is a valuable diagnostic procedure since it demonstrates absence of cardiomegaly and the thick shaggy pericardial sac which characterizes the pathologic findings. Histologically, the lesion, identical with tuberculous

3

Clinical aspects of pericarditis and constrictive pericarditis

HERBERT ELIAS AND LINN J. BOYD

ACUTE AND SUBACUTE PERICARDITIS

Incidence. The exact incidence of pericarditis is difficult to determine since clinical statistics are notoriously unreliable and necropsy reports may be misleading unless a special search is conducted for mild and inactive forms. Necropsy statistics report low figures for acute pericarditis alone and high figures when adhesions and milk spots are included This probably explains why the authors found—reviewing the necropsy reports of the last five decades in several countries—variations from 15.1 to 1 7 per cent. According to Scherf and Boyd (1947), there was an incidence of 3.7 per cent of pericarditis among 36,743 necropsies and according to Smith and Williams (1932), 4 2 per cent among 8,912 necropsies Among 373 cases of pericarditis, 58 per cent were acute (28 per cent fibrinous and 30 per cent exudative) and 42 per cent chronic Males were more frequently affected than females (3,1).

While progress in the therapy of infectious diseases and rheumatic fever has reduced the morbidity and mortality rate of pericarditis, refined laboratory techniques, such as electrocardiography, electrokymography, angiocardiography, cardiac catheterization, and chemical and immunologic tests (antistreptolysin, etc), have uncovered many previously overlooked cases. However, the actual autopsy incidence of pericarditis has changed very little (Griffith and Wallace). The incidence of *bacterial pericarditis* has definitely decreased during the era of chemotherapeutic and antibiotic agents, particularly with respect to tuberculous and pneumococcic forms Pericarditis secondary to *uremia, cardiovascular diseases,* and malignancy has become more common as the number of older people has increased. According to some clinical reports, *nonspecific idiopathic pericarditis* has become the most frequent type, while *rheumatic pericarditis* is now in the second place. A recent study correlating the types of pericarditis with age is shown in Table 8-2.

Causes. A host of factors may cause *fibrinous, serofibrinous,* and *serous* pericarditis. Each variety will not be discussed separately, although a specific etiology tends to provoke a certain type.

Inflammation of the pericardium may be caused by *physical* and chemical agents. Pericarditis may result from *blunt trauma* to the anterior chest without penetration or fracture, from focal increase in temperature (diathermy), or from exposure to *x-ray, radium,* etc. Pericarditis may be provoked by *chemicals* (silicosis, asbestosis, etc). In addition to infectious pericarditis, there are forms of *unknown origin* (in lupus erythematosus, Still's disease, Felty's syndrome, etc.), while others are probably caused by *metabolites* (abnormal in amount or kind), e g, uremic, gout, leukemic, and neoplastic pericarditis (Table 8-2).

Hemorrhagic pericarditis is encountered in primary or secondary tumors, tuberculosis,

pearance. To this end, proper consideration must be given to the state of the myocardium and endocardium, to the presence of systemic infection, and to the status of renal function. Preble (1901) found that acute pericarditis (244 cases) was due to pneumonia in 34 per cent, rheumatic fever in 28.4 per cent, uremia in 11 per cent, tuberculosis in 10 per cent, sepsis in 4.7 per cent, aneurysm (probably including myocardial infarction) in 2.6 per cent, typhoid fever in 1.7 per cent, and other causes in 7.6 per cent of cases. Better control of bacterial infectious processes is reflected by Griffith and Wallace's recent analysis in which *nonspecific idiopathic pericarditis* was most frequent. Pathologic findings, of course, do not reflect the frequent occurrence of acute benign pericarditis, a self-limited process, often with coexistent pleuritis, possibly viral in origin, which may mimic coronary occlusion or acute abdominal disease. *Uremia* and *myocardial infarction* generally produce a sterile fibrinous reaction without significant effusion.

Rarely *acute rheumatic carditis* may be the cause of a hemorrhagic effusion; more commonly, the reaction is predominantly fibrinous. Microscopically, foci of fibrinoid necrosis and nodular infiltrates, analogues of Aschoff bodies, may be found in the epicardium in addition to the nonspecific organizing inflammatory reaction beneath the fibrin deposits. The process may also extend into and involve the contiguous mediastinum and accounts for the development of infrequent cases of *adhesive mediastinopericarditis*, in which dense fibrous adhesions bind the heart and its adherent pericardium to the anterior chest wall and lungs. The cardiac embarrassment which accompanies this condition is attributable to the chronic valvular disease which is invariably present and must be distinguished from constrictive pericarditis.

Acute nonspecific pericarditis is synonymous with *acute benign or acute idiopathic pericarditis;* less frequent terms are acute relapsing, fugitive, or cryptic pericarditis. As the name implies, it is a process which runs a brief course and has a uniformly favorable prognosis, though there may be one or more relapses. Males are affected more than three times as often as females, though no age group is exempt, it is more often observed in the second to fourth decades. Virtually all patients have chest pain aggravated by breathing and movement, chills and fever, mild leucocytosis of variable duration, and an elevated sedimentation rate. In most cases, there is a history of an antecedent upper respiratory infection and there are coexistent signs of pulmonary or pleural disease. In 60 to 75 per cent of cases, a *pericardial friction rub* may be heard at some time during the course of the illness. An effusion is detectable in somewhat more than a third of cases. Duration of illness varies from 2 weeks to 3 months. Relapse is a frequent occurrence and took place in about one-third of Scherl's cases. Electrocardiograms are of considerable diagnostic value and, with the determination of serum transaminase levels, should help in distinguishing the condition from myocardial infarction. Assessment of treatment is difficult because all patients recover without sequelae.

Tuberculous pericarditis, always secondary to an extrinsic focus, usually in the mediastinum or pleura, produces a massive effusion up to 3,500 ml, which at times may be hemorrhagic or fibrinous. According to Spidick, 7 per cent of acute pericarditis is tuberculous and is found in 2.5 to 7.8 per cent of tubercular autopsies. The disease is three to four times more frequent in males and affects all age groups. The greater frequency among Negroes reflects only the higher prevalence of pulmonary tuberculosis. The acute phase may be relatively symptomless, and difficulties arise only with chronicity and the development of constrictive pericarditis. In the absence of tamponade, constitutional symptoms of an effusion are slight. Cardiac embarrassment is related more to the rapidity of accumulation than its size, fluid reaccumulates rapidly after a tap. The fluid is invariably *hemorrhagic*, with a predominance of lymphocytic and mononuclear inflammatory cells. The protein content is usually high, but Andrews et al. did not find that

nosis generally requires culture or animal inoculation. *Pneumopericardium* and x-ray examination is a valuable diagnostic procedure since it demonstrates absence of cardiomegaly and the thick shaggy pericardial sac which characterizes the pathologic findings. Histologically, the lesion, identical with tuberculous

quisite hyperesthesia which precludes percussion and auscultation. The severity of the pain, of course, *is no indication* of the gravity of the underlying lesion. Pain may vanish when an effusion forms and return when the effusion is absorbed.

INSPECTION, PALPATION, PERCUSSION In *uncomplicated fibrinous pericarditis, inspection* may reveal no abnormalities. Palpation may reveal a fine or rough "purr" synchronous with the *friction rub*. This "friction fremitus" is limited *to a small area,* is *superficial,* occurs shortly after the apical impulse, and is often diphasic. The palpatory findings depend greatly upon the position of the patient and *the pressure* exerted by the palpating hand. Strong pressure *may* increase the local distress. Percussion has no diagnostic value in the absence of valvular lesions or pericardial effusion.

AUSCULTATION AND RELATED SIGNS The diagnosis of fibrinous pericarditis is frequently confirmed by discovering the *friction sound.* Like a pleural friction sound, the pericardial rub develops when two layers of the rough, inflamed, and *fibrinous pericardium shift* on one other. It is louder in the left lateral recumbent position. It may be heard even in the presence of a considerable pericardial exudate. The friction rub has no specific etiologic *significance*. It has been described as purring, scratching, rasping, rustling, a whiff, grating, rough, parchment-like, like the creak of new leather or the crunch of snow. It may not be heard; Cabot noted it in only 20 per *cent of his patients*.

Most pericardial rubs are heard between the third and sixth ribs to the left of the sternum, approximately within the area of absolute cardiac dullness. The rub may, however, be audible in other areas. *It may be loudest* in inspiration *or in* expiration, its timing is synchronous with the heart beat and independent of the respiratory phase. This *fact* has some diagnostic value. In contrast with cardiac murmurs, there is no *strict correlation* with any given cardiac phase, and increased pressure *with the bell of the* stethoscope usually *increases* the intensity of the rub. Since the fibrin deposits on the pericardium change rapidly in size, shape, and amount, *the rub* changes rapidly in time and place. The friction rub usually begins shortly after the 1st sound, is loudest *in late systole* and most intense in systole. *In diastole, another rub closely* follows the 2d sound but may occur somewhat later. Not rarely a *presystolic rub* is heard during *atrial contraction.* This results *in a triple* sound. A polyphasic pericardial rub *combined* with the heart sounds is known as the *locomotive murmur* and may, of course, change with altered position.

A misleading "friction sound" may be created by improper application of the stethoscope whereby the diaphragm, riding on two ribs, receives the impact *from an intercostal* space ("pseudo-friction rub") *(Schnur).*

A few other sounds may be confused with a friction rub. A *pleuropericardial rub* may be *heard along the borders of the heart. Pericardial-peritoneal rubs* (acute perihepatitis) usually are encountered near the lower end of the sternum. In early fibrinous pericarditis, a *faint grating systolic bruit may* be *associated* with intense accentuation of the 2d pulmonic sound *(Josserand's sign)* when deposits of fibrin are located anteriorly and pressure in the pulmonary artery *is increased. A squeaky,* high-pitched *systolic* apical sound *(bleat murmur)* may be heard when small strands of exudate bridge the pericardial cavity and become tense during systole.

Laboratory Findings. Associated with the fever and dehydration in fibrinous pericarditis, the *urine* may be more concentrated and darker. The febrile *albuminuria rarely exceeds* 0.1 per cent. The *urinary sediment may* contain *some* hyaline casts, epithelial cells, and a few red blood cells. After the illness subsides, renal function becomes *entirely normal.*

Course and Prognosis. These are *determined* by the *underlying* disease. Fibrinous pericarditis *may heal* without adhesions after 8 to 10 *days;* it *may* change to exudative pericarditis and as such may last for weeks and months. *Therapy* depends entirely upon the *etiology of this condition.*

EXUDATIVE PERICARDITIS

Since *pericardial effusion* often starts as a "dry" pericarditis, the early symptoms and signs of both may be the same. Under these circumstances, the effusion may increase for a time, then gradually subside, and leave some

volvement sufficient, at times, to result in otherwise inexplicable cardiac failure.

Despite the protection afforded by the rib cage, sudden forceful *thoracic compression* may, without bony injury, produce an *acute pericarditis with hemorrhagic effusion.* This is a result of *myocardial contusion* underlying the impact site or contrecoup overlying the vertebral column on the opposite side of the heart. The degree of pericardial injury may, at times, be extensive enough to eventuate in *constrictive pericarditis.* In this regard, Ehrenhaft and Taber have demonstrated the capacity of blood lipid fractions to induce constrictive pericarditis in dogs. In man, Creech et al. considered a high level of cholesterol in the pericardial fluid as the causative factor in a case of constrictive pericarditis. The term "cholesterol pericarditis," however, has dubious diagnostic value. Cholesterol may be found in any body effusion; values are generally lower than the serum level but increase with it, as in myxedema or with hemorrhage or tissue destruction.

In view of current interest in the collagen diseases, it would be an oversight not to mention the frequent occurrence of *pericarditis in disseminated lupus erythematosus,* ranging from diffuse or focal fibrinous to obliterative fibrosis Often the pericardium shows a gelatinous appearance, a gross expression of the increase of mucoid ground substance which accompanies the fibrinoid degenerative changes. Although clinically manifest acute episodes of pericarditis are not a feature of rheumatoid arthritis, Sokoloff found healed pericarditis to be seventeen times as frequent in patients suffering from this disease as in other individuals An effusion of high protein and low cellular content has been reported in *scleroderma,* though it is not a constant feature of the disease Very rarely, since only three cases have been reported, all in obese individuals, pericardial fat necrosis has presented clinically with acute low anterior chest pain and a radiologically visible mass near the cardiac shadow.

CONSTRICTIVE PERICARDITIS (CONCRETIO CORDIS)

That form of chronic adhesive pericarditis which envelops the heart in a thick layer of dense fibrous tissue and thereby interferes with cardiac pulsation is known as "constrictive pericarditis." According to Burwell,

> While there may be some limitation to systolic emptying, the major dysfunction in these patients is a restriction of diastolic filling. This restriction leads to a limited and essentially fixed stroke volume and to a persistent high ventricular filling pressure on both sides of the heart. This pressure is inevitably reflected in high venous and capillary pressures in both the peripheral and pulmonary circuits. The restricted stroke volume usually leads to a low cardiac output per minute in spite of tachycardia.

Historically, cases recognizable as constrictive pericarditis were described as early as 1669. Several reports appeared during the nineteenth century, among them that of Pick (1896), who noted the similarity of the clinical findings to cirrhosis. However, as shown by Volhard and Schmieden (1923), it was the recognition of the importance of cervical venous engorgement and an unenlarged but poorly pulsating heart that permitted the diagnosis to be made during life. Their awareness of the mechanical handicap imposed by the thickened adherent pericardium led them to recommend its resection as a therapeutic procedure. Since then, pericardiectomy has become the standard method of treatment

It is important to recognize that *adhesive pericarditis* is not synonymous with the *constrictive form.* Chevers (1842) observed that the former was associated with enlarged hearts and valvular lesions, whereas small hearts without valve damage characterized the latter The clinical insignificance of simple pericardial adhesions has long been appreciated. *Histologically, constrictive pericarditis is characterized by the formation of a thick layer of dense, avascular, poorly cellular hyaline fibrous tissue fusing with and incorporating visceral and parietal layers* Often the process extends to the very surface of the myocardium at the expense of epicardial fat and even, at times, into the myocardium itself. Small loculated residua of the pericardial space may be found infrequently. Nodular or platelike calcium deposits occur in the majority of cases. Since, in most cases, there is little or no cellular infiltration, it would seem that the lesion is the end result of a widespread destructive inflammatory process. By contrast, the *adhesions,* in nonconstrictive forms of adherent pericar-

quisite hyperesthesia which precludes percussion and auscultation. The severity of the pain, of course, is no indication of the gravity of the underlying lesion. Pain may vanish when an effusion forms and return when the effusion is absorbed.

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ling and Humphreys' cases was attributed to rheumatic pericarditis. It is pertinent to recall that Volhard and Schmieden distinguished adhesive *mediastinopericarditis* (or *accretio cordis*) associated with rheumatic valvular heart disease from *constrictive pericarditis* (or *concretio cordis*), in which valvular heart disease is absent. Uncommonly, *suppurative pericarditis*, rarely *the reaction to myocardial infarction* or to *metastatic carcinoma*, may result in constrictive pericarditis. Long-standing *idiopathic pericardial effusion* may eventually lead *to cardiac constriction.*

The common factors in these varied conditions are, "(1) Prolonged exposure of the pericardium to irritant or damaging agents; tuberculous infection, foreign bodies, or partially organizing blood clot are examples, (2) Extensive pericardial involvement rather than discrete localization" (Deterling and Humphreys).

Other Pathologic Findings. Hydrothorax, often bilateral, and *ascites* are frequent findings in constrictive pericarditis. As distinguished from ordinary congestive heart failure, *in typical cardiac constriction there is a tendency for ascites to precede edema, and the degree of ascites and edema is often striking before shortness of breath causes physical incapacitation* Indeed, as Pick had emphasized, chronic constrictive pericarditis can simulate primary hepatic disease, especially since there is usually *hepatomegaly* as well At autopsy, the liver is uniformly abnormal, in the great majority of instances it is *cirrhotic*, and many times *perihepatitis* is present as well. The cirrhosis is "cardiac" in type, including (Paul et al) *portal* as well as *central fibrosis* There is a moderate *congestive splenomegaly* and a *perisplenitis* in most cases; in a few cases there is *chronic peritonitis*. In most instances, such peritoneal reactions are secondary to the irritant effect of long-standing fluid accumulations and frequent taps. This, however, is not the explanation for the almost uniform presence of a chronic, and at times obliterative, *nonspecific pleuritis*, which may be the chief cause of residual difficulty after surgery. Paul et al. found active pulmonary tuberculosis in only one of their 16 cases. It is *noteworthy that this is far less frequent than* is true of cases of constrictive pericarditis resulting from tuberculous polyserositis.

Treatment is surgical and is designed to remove the constricting tissue. To avoid pulmonary edema, the left ventricle should be cleared first. Without surgery, there is no improvement and slow deterioration. Following operation, most patients *improve to normal* or nearly normal activity, but are left with some residual hemodynamic abnormality.

As listed by Burwell, the following factors determine operative success:

1 Extent of removal of the constricting scar
2. Presence or absence of continued infection
3. Extent to which there is complicating myocardial fibrosis.
4. Presence or absence of constrictive pleuritis, a factor in 50 per cent of patients
5 Congestive cirrhosis and diminished liver function
6. Atrial fibrillation
7 Accessory diseases or conditions such as obesity, pregnancy, valvular heart disease, renal or *pulmonary disease*
8. The postoperative development of hypertension

reveal a definite gradient between the pressure of the cava and that of the right atrium (River et al; Wilson et al).

PERCUSSION. When the pericardial effusion attains a certain size, the *area of absolute dullness approximates that of relative dullness* and the normal dull percussion sound over the heart turns to flatness unless adhesions anchor the lungs to the heart and prevent pulmonary displacement The rapid increase and widening of the cardiac dullness is characteristic of an acute effusion The outline of cardiac dullness, which ends fairly abruptly along the lateral heart borders, becomes triangular or globular Widening to the right may cause the cardiohepatic angle to become more obtuse (*Rotch's sign*) Dullness often extends both to the right beyond the sternum into the 5th right intercostal space and to the left, particularly caudad to the apex beat (*signe de Gendrin*) As pericardial effusion increases, the left border becomes more horizontal and the cardiac dullness becomes rectangular rather than triangular Also characteristic for a pericardial effusion is the changing dullness with change of position. The lower transverse diameter is broad when the patient is erect and decreases in recumbency (Skoda) The dullness may extend to the left or right when the corresponding lateral decubitus positions are assumed Since a pericardial effusion compresses portions of the lungs, tympany may be present above the dullness, particularly in the left anterior chest With greater compression "tympanic dullness" or bronchial breathing may be noted on the left, posteriorly Ultimately the lung behind the heart may become airless and a complete dullness appears, particularly in children (*Pins'* or *Ewart's sign*)

Percussion of the abdomen may reveal a decrease of Traube's semilunar space Recognition of ascites may be difficult if there is edema of the abdominal walls Roentgenologic examination provides greater details than percussion

AUSCULTATION Increasing pericardial effusion muffles the heart sounds as fluid is interposed between the heart and chest wall. Concurrent myocarditis may also contribute to *faintness of the heart sounds* Marked change in the intensity of heart sounds on change of the patient's position speaks in favor of a pericardial effusion

Neurologic Signs. Irritation of the phrenic nerve may cause spasm of the diaphragm and tormenting, exhausting *hiccough*. Pressure exerted by the distended pericardial sac (or possibly the dilated pulminary artery) on the recurrent laryngeal nerve may produce *hoarseness.*

Laboratory Findings. The kidneys exhibit all the signs of congestion, particularly albuminuria and the characteristic sediment in the urine[1] Furthermore, the agent responsible for the exudative pericarditis may also injure the kidney. The albumnuria may be massive. Doubly refractile crystals and granular, fatty, and even waxy casts may be seen in the sediment, but red blood cells are rare. Hypoproteinemia with a low serum albumin may be present. The nonprotein nitrogen level in the blood is normal.

SUPPURATIVE PERICARDITIS

The incidence of this type of pericarditis has markedly declined with the use of antibiotics The signs and symptoms are the same as in any form of severe pericarditis, but the picture becomes extremely grave, with spiking fever, chills, profuse sweating, and severe toxemia Dyspnea and precordial distress are the most constant symptoms.

Physical examination must be very thorough. In only 25 out of 100 fatal cases of purulent pericarditis in children did the amount of pus exceed 90 ml Since the pus tends to collect in the posteroinferior pericardial recess, the area of precordial dullness may not be increased Discovery of a friction rub is rather infrequent even with large effusions. If there is an absolutely flat percussion sound over the precordium, this finding is significant. Enlargement of the liver is not rare and is sometimes combined with slight rigidity and tenderness of the upper abdomen *Cardiac tamponade* with distended neck veins and a small, irregular, and rapid pulse also occurs The general and local symptoms may vary in

[1] Experimental studies have been made (Metcalfe et al., Fishman et al) to investigate the mechanism of edema formation in chronic pericarditis with effusion, peripheral and central venous pressure rise with intrapericardial pressure and induces edema formation by decreasing sodium and water excretion through an increased tubular reabsorption

TABLE 8-2. CAUSE AND INCIDENCE OF PERICARDITIS

Age	Rheumatic	Pyogenic	Tuberculous	Nonspecific	Uremic	Neoplastic	Collagenous	Total
0–9	6 15.0%	3 15%	1 14%	0	1 9%	0	0	11 12.1%
10–39	24 62.5%	2 10%	4 58%	5 50%	2 18%	3 100%	2 100%	42 46.1%
40–59	5 12.5%	9 45%	0	4 40%	6 54%	0	0	24 26.1%
60 up	4 10%	5 25%	2 28%	1 10%	2 18%	0	0	14 15%
Total	39	19	7	10	11	3	2	91

SOURCE: From Reeves, 1953

rheumatic fever, trauma with and without infection, hemorrhagic diatheses, leukemia, nephritis with uremia, sepsis, pneumonia with empyema, aneurysm, avitaminosis, alcoholism, recurrent pericarditis of any kind with fragile granulations, cholesterol pericarditis, and in epicarditis chronica pigmentosa superficialis and xanthomatosa.

Suppurative pericarditis as a rule is caused by organisms being conveyed by pulmonary and pleural lymphatic system (This source accounts for 50 per cent of the cases.) The frequency of suppurative pericarditis depends, of course, on the particular country (it is more common in China), the era (common in the influenza epidemic of 1918-1919 associated with pulmonary infections), and the types of patients studied (higher incidence in studies of patients who were observed on surgical services).

FIBRINOUS PERICARDITIS (PERICARDITIS SICCA)

Fibrinous pericarditis is the commonest and least serious form of pericarditis, accounting for about 50 per cent of the cases. Although never lethal per se, fibrinous pericarditis accompanies many serious diseases The pericarditis may be fleeting, but it may be only one manifestation of a serious rheumatic pancarditis which continues for months.

Symptoms and Signs. Cardiac symptoms may be absent or may be overshadowed by the symptoms of the attendant disorder. Only slight fever may herald the insidious onset In other cases, fibrinous pericarditis starts abruptly with a *chill, restlessness,* and perhaps a little *shortness of breath.* The breathing may become shallow and the face pale, reflecting distress or anxiety. *Precordial oppression* may be mentioned. Early *nausea* and *vomiting,* usually a later sign, often suggest a poor prognosis. If the patient is not thoroughly studied, the symptoms may mistakenly be assigned to some other process.

PAIN. Over one-half of the patients are reported to complain of pain. It is often difficult to decide how much an accompanying pleurisy contributes to the pain. The classical pain is felt in the 4th or 5th left intercostal space. Retrosternal or neck pain occurs when the anterior mediastinum or the diaphragmatic pleura is involved With posterior mediastinopericarditis or dorsal pleuritis, back pain oc-

[illegible]

ing so that the patient avoids swallowing (pericarditis hydrophobica). The distress may be greatly increased by rotation of the trunk, and the patient may be tormented by distressing *hiccoughs* (Capps and Coleman). The severe, sticking, or lancinating *pain* may be accentuated by *cough.* Since breathing aggravates the pain, respiration becomes shallow, and *dyspnea* and *cyanosis* may develop Sometimes the pain is associated with an ex-

neuralgia, nonparalytic poliomyelitis, appendicitis, or cholecystitis may be mistakenly suspected (Powers et al).

However, examination usually reveals the characteristic outstanding sign of this condition, i e , the pericardial friction rub. The diameters of the cardiac shadow may enlarge decidedly, sometimes within 12 hr. The venous pressure rises slightly, but paracentesis usually is unnecessary even though the enlargement and the fever may persist for 2 or 3 weeks. Tamponade is rare. A concomitant pleural effusion may occur Such episodes are repeated in 30 per cent of the patients (Tomlin et al., Goyette). The mild leucocytosis usually vanishes within the first week of the illness, and the increased sedimentation rate returns to normal in 1 or 2 weeks. The size of the pericardial effusion may be large. The fluid has a specific gravity around 1 020, a high lymphocyte count, and may be hemorrhagic.

The ultimate prognosis in these patients is, for the most part, excellent, but residual electrocardiographic abnormalities were found in 6 out of 50 cases (Carmichael et al.); ultimate constrictive pericarditis seems to be rare (Krock; Sturup, Rabiner et al , Frelich)

Two conditions in particular must be considered for the differential diagnosis in young patients, rheumatic pericarditis, and in middle-aged and older persons, infarction pericarditis In acute nonspecific pericarditis there is no history of previous rheumatic fever or previous cardiac attack, no endocardial murmur, no joint pain or swelling, and salicylates give no relief; in rheumatic pericarditis one often hears of previous attacks of rheumatic fever, there may be blowing heart murmurs, polyarthritis, etc , and salicylates definitely relieve the pain (Friedman et al) In infarction pericarditis, fever and a friction rub appear much later than in nonspecific pericarditis, where the latter may be audible a few hours after onset In infarction pericarditis, it is uncommon for the pain to be intensified by respiration, torsion of the body, swallowing, coughing, as described in nonspecific pericarditis, transaminase rises sharply, and the ECG has typical features

TREATMENT. Under the assumption that acute nonspecific pericarditis is caused by a virus, antibiotics have been administered, particularly *Aureomycin* (Taubenhaus and Brams; Bower et al.), but Verhayden used it in three cases without obvious effect. ACTH and cortisone do not change the eventual course of the disease but do bring about immediate relief. Analgesic drugs are often needed.

Tuberculous Pericarditis. Pulmonary or hilar lymph node tuberculosis was found in 65 out of 143 cases, and regional tuberculous lymphadenitis could have been responsible in 36 more, apart from several cases of miliary tuberculosis. Primary tuberculous pericarditis may occur in elderly patients The following analysis of 340 cases proves the multiplicity of forms of tuberculous pericarditis: adhesive, 212; serofibrinous, 62; caseous, 18; serous, 15; purulent, 7; necrotic, 5; miliary, 5; hemorrhagic, nodular, or simple fibrinous, each 4; pyopneumopericardium and chylopericardium, each 2. Acute tuberculous pericardial effusion may vary from small (50 to 200 ml) to enormous (up to 4,000 ml). The fluid may be sometimes rose-red, current-jelly-like, dark brown, or straw colored with fibrinous flakes. Purulent pericardial fluid is not common in the absence of a secondary infection. The pus may be gritty, containing small calcareous concretions. The specific gravity of the serous effusion varies but is usually above 1.018. In nonpurulent effusions, lymphocytes usually predominate, but this is not pathognomonic for tuberculosis Immediate demonstration of the tubercle bacillus by direct smears may be possible. Usually culture or guinea pig inoculation for the confirmation of the diagnosis is necessary, but the results may also be negative.

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Symptoms and Signs. The onset may be abrupt or insidious, with *pain, fever, restlessness,* and *insomnia.* The temperature depends upon the type and intensity of the inflammation. While tuberculous effusions are usually associated with a typical afternoon rise of temperature, persistent fever or absence of fever is also observed. On the other hand, the transition of a tuberculous serous effusion into a pyopericardium may produce a spiking type of temperature. The precordial temperature in exudative pericarditis is often higher in comparison to the right chest side; the difference, according to thermocouple readings, amounts to about 2°F (1.4 to 2.7°F). After absorption of the exudate, this difference may vanish (Elias).

INSPECTION. As the effusion increases, *dyspnea* occurs, the patient tends to sit up and lean forward. In other cases, the patient may place a pillow on the flexed knees and clasp his arms around his legs. The face is turned aside, and an ear rests on the pillow (*sign of the pillow*). The patient may even adopt the *knee-chest position* in order to obtain relief. At times, a large effusion causes esophageal compression and irritation and *dysphagia* with interscapular pain. This dysphagia is aggravated by the recumbent position and relieved by sitting up.

The *face* is apprehensive, distressed, pale or pale-cyanotic. The cyanotic face of the patient sitting on the edge of the bed with his protruding eyes expresses a sense of impending doom; the forehead is covered with cold sweat, the nares are dilated—an unforgettable picture. Obstruction to venous return to the heart may produce *edema of the face* extending to the neck and upper extremities, and because of congestion of the cerebral vessels, there may be vertigo, ringing in the ears, *delirium,* and even *syncope. The neck veins may remain engorged even in the upright position* and do not collapse during inspiration. Pressure on the abdomen causes further distention of the jugular veins (*hepatojugular reflex*), but with extreme jugular distention, this sign disappears. There may be an enlargement of the left thorax with large effusions, particularly in children, and even a protrusion of the lower xiphoid (Auenbrugger). The apical impulse often is invisible. The intercostal spaces become more horizontal and may even protrude owing to the accompanying pleural effusion. The upper abdomen, particularly the right upper quadrant (and sometimes the entire abdomen), may appear distended. Dilated veins may be seen beneath the skin of the abdomen when the patient is neither obese or edematous. A very large, acutely congested and therefore pressure-sensitive liver—sometimes with mild jaundice—is usually present and, together with meteorism, causes great discomfort. Edema of the extremities is not rare if the effusion is large and rapidly increasing. Drumstick fingers and toes occur with long-standing pericardial effusions.

PALPATION. Usually the radial pulse is small, fast, and easily compressible, and sometimes weaker in the left wrist (Potain). The intercostal spaces offer more resistance to pressure on the left side. As the volume of the pericardial exudate increases, greater pressure is exerted on the lower lobe of the left lung. At the beginning, when this lobe retains some of its air, tactile fremitus may be locally increased, later when the lobe is almost completely compressed and displaced, *tactile fremitus may vanish completely.* The apical impulse, if palpable, lies *within* the area of cardiac dullness and is shifted medially and upward, the exudate collecting in greater amount between the depressed diaphragm and the heart. In some positions a distinct substernal grating rub may be felt despite a considerable collection of fluid in the sac. The upper border of the first rib may become palpable owing to elevation of the clavicle from increased respiratory effort (*sign of Ewart*).

Palpation of the abdomen often reveals an *enlarged, firm, smooth, and tender liver* extending almost to the umbilicus, often as early as the first or second day of illness. It was suggested that this characteristic sign could be explained by pressure of the pericardial exudate on the weak wall of the intrapericardial supradiaphragmatic orifices of the hepatic veins and of the inferior cava (Elias and Feller). However, catheterization studies failed to

neuralgia, nonparalytic poliomyelitis, appendicitis, or cholecystitis may be mistakenly suspected (Powers et al.)

However, examination usually reveals the characteristic outstanding sign of this condition, i.e., the pericardial friction rub. The diameters of the cardiac shadow may enlarge decidedly, sometimes within 12 hr. The venous pressure rises slightly, but paracentesis usually is unnecessary even though the enlargement and the fever may perist for 2 or 3 weeks. Tamponade is rare. A concomitant pleural effusion may occur. Such episodes are repeated in 30 per cent of the patients (Tomlin et al.; Goyette). The mild leucocytosis usually vanishes within the first week of the illness, and the increased sedimentation rate returns to normal in 1 or 2 weeks. The size of the pericardial effusion may be large. The fluid has a specific gravity around 1.020, a high lymphocyte count, and may be hemorrhagic.

The ultimate prognosis in these patients is, for the most part, excellent, but residual electrocardiographic abnormalities were found in 6 out of 50 cases (Carmichael et al.), ultimate constrictive pericarditis seems to be rare (Krock, Sturup, Rabiner et al., Frelich).

Two conditions in particular must be considered for the differential diagnosis: in young patients, rheumatic pericarditis, and in middle-aged and older persons, infarction pericarditis. In acute nonspecific pericarditis there is no history of previous rheumatic fever or previous cardiac attack, no endocardial murmur, no joint pain or swelling, and salicylates give no relief; in rheumatic pericarditis one often hears of previous attacks of rheumatic fever, there may be blowing heart murmurs, polyarthritis, etc., and salicylates definitely relieve the pain (Friedman et al.). In infarction pericarditis, fever and a friction rub appear much later than in nonspecific pericarditis, where the latter may be audible a few hours after onset. In infarction pericarditis, it is uncommon for the pain to be intensified by respiration, torsion of the body, swallowing, coughing, as described in nonspecific pericarditis, transaminase rises sharply, and the ECG has typical features.

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may be confirmed by fluoroscopy and roentgenograms taken with the patient in different positions and in different phases of respiration (see below) or by tomography. The restriction of movement of the pericardial fluid with shift in body position thus becomes apparent Paracentesis with injection of air may permit visualization of different compartments, but this procedure is inadvisable. Owing to the lack of symptoms, the discovery of such "inflammatory diverticuli" is often accidental. Marked widening of cardiac dullness to the right with diminished mobility of the adjacent lung has been noted

The residual exudate may conform with the cardiac surface but usually assumes a peculiar globular shape along the right border. On fluoroscopy it elongates and narrows during inspiration and becomes broad as well as "plump" in expiration (*Jansen's sign*) This sign is also seen with pericardial cysts and even in cholesterol pericarditis. Pulsation is an important sign of encapsulation of an effusion, its intensity depending, of course, upon the extent of cardiac motion, the proximity of the sac to the heart, the presence or absence of thick scars, and the size of the communication between the pocket and pericardial sac If the neck of the sac is wide, open powerful pulsation may be transmitted. The differentiation from true pericardial diverticuli may be difficult or impossible

Usually treatment is unnecessary. If infection or pressure causes symptoms, pericardiostomy or partial pericardiectomy may be necessary

Myocardial Damage. Myocarditis usually accompanies pericarditis This epimyocarditis is particularly severe in coccal infections and in uremic pericarditis, in tuberculous myocarditis, the alteration in the myocardium may range from trivial to extensive.

LABORATORY FINDINGS

Roentgenology. In "dry" fibrinous pericarditis, exudate is not demonstrable by x-ray

In exudative pericarditis, small effusions (below 250 to 500 ml in adults) are not detectable by x-ray On the other hand, as little as *10 ml* may cause changes in infants Although certain x-ray signs are strongly suggestive of pericardial effusion, no particular cardiac silhouette is pathognomonic of pericardial exudate Usually the cardiac shadow

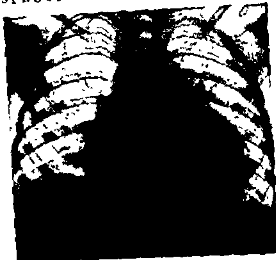


Fig. 8-1. Anteroposterior view of a case with pericardial effusion. Note light lung fields and the acute cardiohepatic angle.

is increased in its transverse diameter, particularly in its lower two-thirds, and especially to the left On deep inspiration, *the transverse* diameter decreases by 1 to 2 5 cm with a moderately large effusion if diaphragmatic action is still preserved.

The form of the cardiac shadow has been compared with a hot water bottle, a barber's bowl, or a large flask when the pericardium is not tightly distended After pericardial tap or partial absorption of the fluid, the shadow may become triangular and will be even more distinctly influenced by altering the position of the body. On the other hand, if the serous pericardium is *tense*, the shadow is rather globular and tends to retain its shape in spite of a change in position. The pericardium distends in its upper portion rather than at its diaphragmatic attachment, so that an acute cardiohepatic angle is preserved in the PA view in contrast to the obtuse angle obtained on percussion (Fig 8-1) The compressed and semiatelectatic paracardial lung wedge is responsible for this difference between the physical and x-ray findings The characteristic landmarks of the cardiac silhouette for the most part vanish early. With an increasing amount of exudate, the edges of the cardiac shadow bend more and more, *forming convex* arcs which finally start on the left *side, shorten* the pedicle so that the median shadow then *resembles a round bottle with* a short neck (*inverted funnel of Assmann*) The left diaphragmatic leaf is pushed downward, and the

intensity, and fever may even be absent. Although the white blood count usually is high (20,000 to 40,000) and the sedimentation rate is increased, such findings are not specific since the underlying disease may cause similar changes. With these signs plus serial roentgenograms, a correct diagnosis is usually possible before paracentesis is performed. However, even repeated pericardial taps combined with vigorous antibiotic therapy may not prevent a fatal outcome.

HEMORRHAGIC PERICARDITIS

In general, hemorrhagic pericarditis presents the same symptoms and signs as exudative pericarditis. Sometimes the condition is difficult to detect, and the diagnosis may be made only after paracentesis. It may be suspected from the history in the presence of a hemorrhagic diathesis or when hemorrhages in the skin or other organs are apparent. Hemorrhagic pericardial effusion may be a complication of anticoagulant therapy. Tapping is done only in case of tamponade.

CHOLESTEROL PERICARDITIS

Cholesterol pericarditis is rare and is encountered in myxedema, tuberculous pericarditis, hemopericardium, and sometimes without demonstrable etiology (Creech et al.). It is characterized by a yellow, sometimes greenish, opalescent pericardial exudate containing a large amount of cholesterol crystals. Except in myxedema, the serum cholesterol is usually normal. The myxedematous type responds to thyroid administration (Lange). Cholesterol pericarditis following hemopericardium is probably due to the lipids remaining after hemolysis and after reabsorption of part of the pericardial fluid Cholesterol pericarditis may be followed by constrictive pericarditis (Creech et al.). Experimentally, intrapericardial injection of lipids causes severe constrictive pericarditis (Ehrenhaft and Taber).

SPECIAL FORMS

Rheumatic Pericarditis. The patients often give a previous history of migrating polyarthritis, recurrent tonsillitis, or chorea; some have no such past history. The onset of rheumatic fever and of pericarditis may be insidious or abrupt A chill may be followed by fever and moderately severe precordial or substernal pain. Nearly 25 per cent of patients with rheumatic pericarditis have no other local symptoms except mild precordial distress. Sometimes the distress may be noted in some unusual area, such as the interscapular region, and may be aggravated by deep breathing, swallowing, etc. The fever usually does not exceed 103°F and is often lower, but may be high in rare cases (106°F).

The *sedimentation rate,* already elevated by the rheumatic process, often shows no further rise with the advent of pericarditis. The white cell count usually ranges from 10,000 to 30,-000, but it may be normal. *Leucocytosis* is usually of short duration, but relative lymphocytosis may persist for several weeks The *antistreptolysin titer* may rise sharply; the *C-reactive protein test* is strongly positive, and a slight febrile albuminuria is usually present.

The heart rate may be slow at the onset, but a *tachycardia* (120 beats per minute) is more usual. Pulse and respiratory rate disproportionate to the fever suggest myocarditis or pancarditis. Conduction disturbances may occur, particularly in children. The friction rub may antedate the arthritis or may become audible a few hours after joint symptoms appear. It may be present for only a few hours and in a very small area.

Acute Nonspecific Pericarditis (Acute Benign Pericarditis, Acute Idiopathic Pericarditis, Pericarditis of Undetermined Origin). This form was probably described first by Hodges (1854) and possibly by Corvisart and Bouillaud This condition may be due to multiple causes. Most authors consider either a virus infection or hypersensitivity as possible mechanisms (Verhayden). The clinical picture shows great similarity to epidemic pleurodynia, but Friedman et al. could not isolate the Coxsackie virus in five cases of acute benign pericarditis.

An antecedent infection of the respiratory tract is common but often is forgotten, unless a special inquiry is made. Thoracic pain may begin with dramatic suddenness, with immediate incapacitation and high fever, or it may be mild or intermittent for several days before it reaches a peak. It is often associated with collapse and with confusing abdominal symptoms (Carmichael et al.). The pain is aggravated by breathing, coughing, twisting the trunk, and sometimes by swallowing. Because of this initial pain, mediastinitis, dissecting aneurysm, diaphragmatic hernia, intercostal

gardless of the etiology. It consists of *low voltage* in all standard leads (Cybulski and Surcycki, 1912) and often in the chest leads. The P and T waves may be flattened. After paracentesis, a normal voltage returns (Scherf). The low voltage is due to short-circuiting of the cardiac potentials. Low voltage may occur in normal persons, but then the P and T waves are of normal height. Low voltage is also found in severe emphysema (electrical isolation of the heart), in brown atrophy of the myocardium caused by starvation, and in myxedema.

Electrical alternans may occur in pericardial effusion (McGregor and Baskind), as well as AV block, atrial fibrillation, and other arrhythmias. These may vanish after paracenteses.

The most typical electrocardiographic changes of pericarditis are caused by the inflammation of the subepicardial layers of the myocardium (Boyd and Scherf, Kisch et al.) There are four characteristic stages (Fig. 8-2)

STAGE OF ELEVATION OF THE RST SEGMENT (up to 3.5 mm). This displacement is often found in all standard leads, even though, following Einthoven's rule, it is most pronounced in lead II, or leads II and III. In a majority of cases the chest leads show the same elevation. This RST elevation is an early sign and may appear before clinical signs of pericarditis are detected.

It is of utmost importance in this stage to differentiate the pattern of pericarditis from that of myocardial infarction since these clinical pictures are often similar and moreover may occur simultaneously.

STAGE OF NORMAL TRACING After some days, the elevation of the RST segment disappears, most particularly in children with rheumatic pericarditis. A single ECG taken during this phase could be misleading.

STAGE OF THE NEGATIVE T WAVES. The T waves gradually become flat, notched, or diphasic and then inverted. They may be deeply

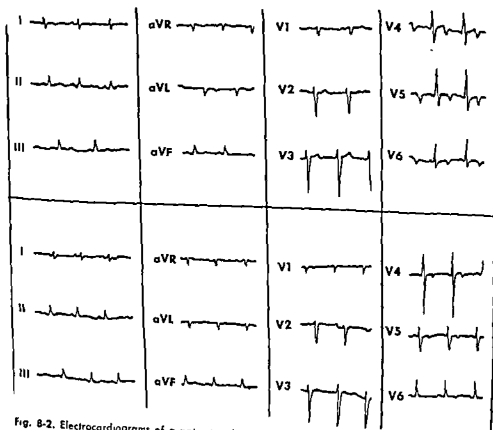


Fig. 8-2. Electrocardiograms of a patient with acute pericarditis. (Above) May 21, 1958. (Below) May 24, 1958

Antituberculous drug therapy must be used and may be the definitive treatment, but many cases require surgical intervention early. Even during antituberculous management, constrictive pericarditis may rapidly develop (Dubourg et al.).

Uremic Pericarditis. This is a common, late toxic complication of uremia. The peak of incidence is between the ages of 35 to 37. Among 300 cases of uremia with pericarditis, a pericardial effusion was present in 61 cases. The pericarditis was of the dry type in 25, serofibrinous in 97, adhesive in 43, hemorrhagic in 3, and purulent in 1.

Almost invariably the underlying renal lesion is evident from the azotemia, hypertension, and all the signs and symptoms of uremia. There is a normocytic normochromic anemia. The white cell count rarely exceeds 15,000; leucopenia with either lymphocytosis or lymphopenia frequently is observed. The usual nitrogen retention and electrolyte disturbances in the blood are present

Fever may or may not occur with the pericarditis Usually uremic pericarditis is painless, but chest discomfort is not rare. Dyspnea may increase with the advent of pericarditis.

Repeated, painstaking examinations disclose a *friction rub* in most cases (Richter). Dorsal friction sounds occur more often in uremic pericarditis than in other forms, probably on account of coexistent pulmonary complications in bedridden patients

Uremic pericarditis may be recognized electrocardiographically, and transient forms, which previously escaped clinical detection, may thus be detected. These patients may recover from their pericarditis (Keith et al.). While the average duration of life after the detection of uremic pericarditis is about 7 to 16 days, some patients may live 2 to 3 months

Rare Forms. In *disseminated lupus erythematosus,* acute pericarditis with effusions of 600 to 900 ml is common There is also frequent pleural and mediastinal involvement.

In *Still's disease,* pericarditis is also not unusual The polyarthritis with high fever may suggest the diagnosis of rheumatic pericarditis, but the latter lacks generalized lymphadenopathy and splenomegaly.

The combination of *Bornholm disease* (*epidemic pleurodynia*) with pericarditis and pleuritis occurs chiefly in young adults. It is a painful but benign disorder.

In *periarteritis nodosa,* hemorrhagic fibrinopurulent pericarditis may occur (Boyd). A biopsy of the skin or muscle may confirm the clinical diagnosis.

Fibrinous pericarditis in *erythroderma desquamativa Leiner* is rather common. This mysterious childhood disease begins with a macular erythema on the trunk. Later, it spreads over the entire body, the skin becomes thick and indurated, and the epidermis is shed in large flakes.

COMPLICATIONS AND SEQUELAE

Complications and sequelae of acute and subacute pericarditis depend on the etiology. A patient with tuberculous pericarditis may develop tuberculous meningitis, while a patient with uremic pericarditis will most probably succumb from his renal lesion.

Adhesions are the most common complication and, if constrictive, may have serious consequences.

A relatively rare complication is the "spontaneous" *seropneumopericardium.* It may occur whenever a gas-containing hollow structure (stomach, intestine, bronchus, pneumothorax, etc.) ruptures into the pericardial sac and infects it or when an anaerobic infection produces gas within it. More frequently, air is introduced in the pericardial cavity, either for therapeutic or diagnostic reasons or unintentionally, during a pericardial tap or through accidental puncture of the pericardium. The clinical picture varies to a great extent with the etiology and also according to the rapidity with which the air or gas enters the pericardial cavity. No apical impulse is palpable in most cases. The pulse may be rapid, small, and irregular In the recumbent position, a tympanitic or metallic sound on percussion replaces the absolute cardiac dullness; this shows a horizontal border in the upright position, ending sharply where the air bubble begins. The outstanding sign on auscultation in about 50 per cent of the cases is a *splashing, continuous, ringing cardiac metallic sound,* the "bruit de moulin" (mill or water-wheel murmur). All these signs change with the position of the patient.

Encapsulated Pericardial Effusion. Ordinarily the recognition of a residual pericardial effusion offers little difficulty when there is a history of recent pericardial disease. The diagnosis of an encapsulated pericardial effusion

gardless of the etiology. It consists of *low voltage* in all standard leads (Cybulski and Surcycki, 1912) and often in the chest leads. The P and T waves may be flattened. After paracentesis, a normal voltage returns (Scherf). The low voltage is due to short-circuiting of the cardiac potentials. *Low voltage may occur* in normal persons, but then the P and T waves are of normal height. Low voltage is also found in severe emphysema (electrical isolation of the heart), in brown atrophy of the myocardium caused by starvation, and in myxedema

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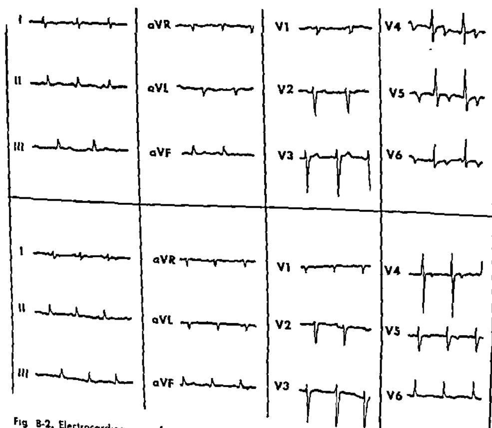


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gastric air bubble may be indented. The right diaphragm is often pushed upward by the enlarged liver.

In the lateral views, the pericardial shadow lies mainly in the anterior chest but may extend backward and encroach on the retrocardiac space. The initial collection of fluid in the lower pericardial recess is often missed (Fleischner), but in exact lateral views, the cardiodiaphragmatic angle is often obscured. If the esophagus is filled with barium, a large pressure concavity may be seen in its lower part (Levine and Kaufman). The pericardial effusion may displace the esophagus backward and to the right. The reduction or even disappearance of pulsations of the cardiac shadow is characteristic, but not pathognomonic, of pericardial effusion since the same picture may be produced by an extremely enlarged heart with severe myocardial damage. A sudden increase or decrease of the entire cardiac shadow speaks in favor of a pericardial effusion in the majority of the cases.

The effect of changes of posture on cardiac shape should be tested in questionable cases when the condition of the patient permits such movements However, the interpretation of these signs is often difficult A central shadow within the shadow of the pericardial effusion is not a reliable sign for it often proves to be of extracardiac origin Good visibility and widening of the angle of the tracheal bifurcation speak in favor of an enlarged left atrium and against pericardial effusion

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Electrical alternans may occur in pericardial effusion (McGregor and Baskind), as well as AV block, atrial fibrillation, and other arrhythmias. These may vanish after paracenteses

The most typical electrocardiographic changes of pericarditis are caused by the inflammation of the subepicardial layers of the myocardium (Boyd and Scherf, Kisch et al) There are four characteristic stages (Fig 8-2)

STAGE OF ELEVATION OF THE RST SEGMENT (up to 3.5 mm). This displacement is often found in all standard leads, even though, following Einthoven's rule, it is most pronounced in lead II, or leads II and III. In a majority of cases the chest leads show the same elevation. This RST elevation is an early sign and may appear before clinical signs of pericarditis are detected.

It is of utmost importance in this stage to differentiate the pattern of pericarditis from that of myocardial infarction since these clinical pictures are often similar and moreover may occur simultaneously.

STAGE OF NORMAL TRACING. After some days, the elevation of the RST segment disappears, most particularly in children with rheumatic pericarditis. A single ECG taken during this phase could be misleading

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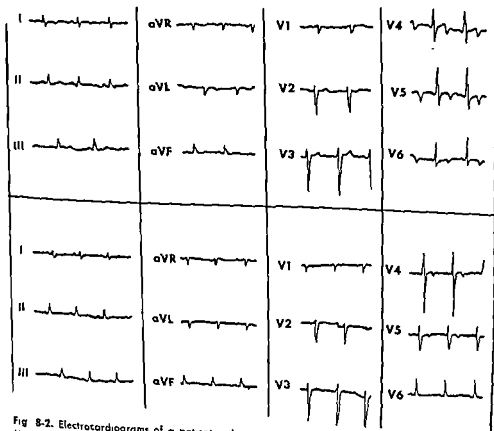


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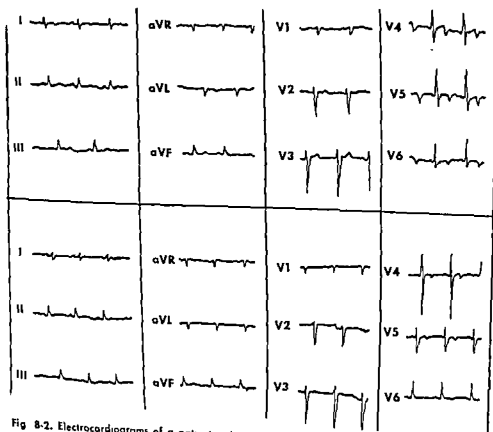


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Pericardial friction sounds	*Endocardial murmurs*
Rubbing	Swishing, blowing
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The diagnosis of pericardial effusion usually does not offer difficulties if the exudate exceeds 300 ml and if the patient is carefully examined In the differential diagnosis between pericardial effusion and a marked cardiac enlargement, absolute flatness, rapid change in size and shape of the dullness, and only slight prolongation of circulation time (Bellet et al) speak in favor of effusion The ECG may be very helpful

Sometimes it is not easy to distinguish a pericardial effusion from a *paralysis of the left leaf of the diaphragm* The two conditions may show similarity if the widespread relative dullness over the anterior and posterior left chest extends beyond the right sternal border and the cardiac apex is elevated The heart sounds are soft over a pericardial effusion and normal or accentuated in left phrenic nerve paralysis, epigastric pulsation is common in pericarditis, absent in left diaphragmatic paralysis, the left lobe of the liver is displaced downward by the effusion and shifted upward with the paralyzed diaphragm This problem in differential diagnosis is of course resolved quickly by roentgenologic examination

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Recently pericardial biopsy has been recommended for the correct diagnosis of pericarditis (Barr, Proudfit and Effler). Pericardiotomy permits direct inspection of the pericardial sac, culture of fluid and tissue biopsy, and when desirable, the establishment of a pleuropericardial window

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Usually, acute fibrinous pericarditis is a local manifestation or complication of a generalized disease (rheumatic fever), of an infection (tuberculosis, etc), of a severe metabolic abnormality (uremia, etc), or of a lesion in the direct neighborhood (myocardial infarction, neoplasm, etc.). Its course and prognosis therefore are determined by the underlying disease *Fibrinous pericarditis* may heal without adhesions and without lasting myocardial damage after 8 to 10 days, or it may last for weeks or months, or perhaps until the end without being responsible for death. If adhesions form, they do not necessarily hamper cardiac efficiency even when complete *concretio* occurs. The situation is different in mediastino- and constrictive pericarditis

The course and prognosis of a *pericarditis with effusion* also depends upon the severity of the underlying disease However, since the formation of fluid is evidence of a more intensive inflammation—particularly when the exudate is purulent—the disease is more *serious* in every respect It may persist for many

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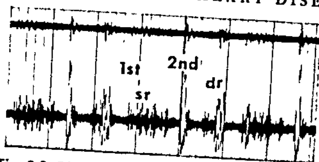


Fig. 8-3. Filtered tracing (band 150 to 250 cps). The phonocardiogram shows pericardial friction rubs in two groups. *s.r.*, systolic rub; *d.r.*, diastolic rub. (Courtesy of A. Luisada.)

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According to Cossio's description, the typical rubs may occur in three phases presystole, early systole, and early diastole, however, they are often found only in two phases of the cardiac cycle (Fig 8-3)

In fibrinous pericarditis, the vibrations of the characteristic systolic-diastolic *locomotive murmur* are registered According to Lian, the ordinary friction rub lasts 0 04 to 0 06 sec, with frequencies of 100 to 150 vibrations per second For comparison, a presystolic gallop usually has only 40 to 50 vibrations per second. Sometimes, however, the vibrations of a friction sound may be of a low frequency also If the rub is a soft, swishing systolic sound, it may be erroneously mistaken for a "vibratory" murmur. The latter is characterized in the phonocardiogram by a regular series of vibrations of constant frequency if the tracings are taken at points distant from the point of maximal intensity (Harris and Friedman).

When an effusion subsequently appears, the friction sound progressively decreases in intensity and may finally vanish. Then, as a rule, the heart sounds become weaker on auscultation. Frequently a 4th (atrial) sound can be registered in exudative pericarditis; this indicates a higher atrial pressure.

Ballistocardiography. Few ballistocardiograms of acute and subacute pericarditis have been published. Winer and Zariello found bizarre patterns with marked respiratory variations in a case of pericardial tamponade.

Pneumotachography. If the oscillations of the air column in the bronchial tree are registered in exudative pericarditis by a standardized pneumotachography, the cardiopneumatic waves appear reduced in proportion to the amount of effusion, while their form and direction are maintained. Since many of the patients suffer from dyspnea or cannot hold the glottis open during respiratory standstill, the method has limited application.[2]

Angiocardiography. The presence of a pericardial effusion in questionable cases can be established by this technique A distance greater than 0.5 cm exists between the contrast medium in the right atrium and the margin of the cardiac silhouette (Dotter and Steinberg). Loculated effusions and tumors can be localized and might be differentiated by combining this technique with Jansen's test Pericardial calcification may be differentiated from myocardial calcification (Dotter and Steinberg) However, this technique should be used only with great care. The patient must not be sensitive to the contrast agent, and all precautionary measures against shock, respiratory arrest, cardiac arrest, pulmonary edema, etc, must be at hand since fatalities following angiocardiography may occur.

DIAGNOSIS

Since the diagnosis of a fibrinous pericarditis is based to a great extent on auscultation, it is important to distinguish a pericardial friction rub from an endocardial murmur. This is usually easy as can be seen from the comparison of murmurs shown in the following list.

[2] Pneumotachography is described in Part 4, Chap 9 *Editor.*

molecules of desoxy-ribonucleoproteins *in pus* and necrotic tissue and facilitates resorption. In the presence of active hemorrhage, this therapy is contraindicated. Repeated injections of small doses (allergic reactions) are advisable.

Unfortunately, cases of pericarditis of unknown etiology are the most *common* (rheumatic or idiopathic). For these conditions, whether fibrinous or exudative, *salicylates* were used for many *decades and were* warmly advocated by Coburn, who stressed *intravenous administration* The authors feel that *the route of administration (oral*, rectal, intramuscular, or intravenous) *is not important* but that *it is important* for the blood level to remain around 20 mg per 100 ml, a level requiring 10 to 13 Gm *daily unless* salicylate intoxication occurs. Although salicylates are rapid and safe analgesics and antipyretics, they *are not specific* in rheumatic fever nor do they prevent polycyclic attacks The same holds for the still faster and more intense effect of ACTH and *cortisone*. With them, fever disappears, friction rub and pericardial effusion vanish (usually within the first week), the patient feels well, but the process slumbers, and when steroid therapy is slowly discontinued the manifestations of rheumatic fever return and the disease takes its unpredictable course At the beginning, *penicillin* is advisable for a few days in order to suppress a possible coccal infection To protect young patients after recovery from rheumatic pericarditis against new streptococcal infections and consequent rheumatic attacks, prolonged use of long-acting *Bicillin* (1,200,000 units, once a month) has proved useful This prophylactic therapy should be administered until the patients pass puberty, and in adults it should be continued for 1 to 2 years after the attack, *or possibly* longer

The pericarditis of *disseminated lupus erythematosus* often remits after the administration of 100 mg *ACTH* daily However, the patients become refractory *to the drug* and do not respond *to a second* or third course (Grace and Combes, Elkinton et al.) In the pericarditis of sarcoidosis, *ACTH and cortisone* may be of value (Dolphin and Heathfield, Shulman et al). For pericarditis in erythroderma desquamativa and in periarteritis nodosa, no successful therapy is known In gouty pericarditis, the gout is treated with *diet and colchicine* (0.5 to 1.0 Gm reduced). There is no definite *treatment* for uremic or carcinomatous pericarditis. In pericarditis following x-ray radiation, this therapy should be discontinued.

An important task is the treatment *of the circulatory disturbances*. Strict *bed rest* should be maintained until all danger is passed. *Digitalis* frequently is administered when the pulse is small, rapid, and irregular. However, cardiac decompensation of the type favorably influenced by digitalis is *not common* in fibrinous or exudative pericarditis. Digitalis seems less effective and requires larger doses in febrile patients. *If pericarditis occurs* with auricular fibrillation or flutter or in a patient with a previously damaged heart and the myocardium stands at *the brink of decompensation*, digitalis may be useful. This, however, is not too common. Myocardial failure, not pericarditis, is treated by digitalis.

If rapid circulatory stimulation is required, *caffein* or *coramine* may be considered; oxygen may be indicated for circulatory collapse, severe dyspnea, or cyanosis. *For the medical* treatment of the edema, the traditional xanthin diuretics or *Diuril* may be used. However, *mercurial diuretics* are often more effective in spite of opposing theoretical reasons. They may be administered orally, in combination with ascorbic acid, or rectally, intramuscularly, or intravenously. The intraperitoneal injection when ascites is present offers no particular advantage. If the patient finally becomes refractory to mercurials, he *may still respond to an exchange resin* The correction of a hypoproteinemia caused by repeated abdominal tapping is also important.

The withdrawal *of fluid from* the pericardial cavity *is* indicated at times for diagnostic and therapeutic purposes

Pericardial tap is indicated *when signs of respiratory or circulatory* embarrassment, such as *increasing* dyspnea, tachycardia, cyanosis, and venous distention, and *particularly a fall* of systolic arterial *pressure, indicate impending tamponade. The removal* of pus in order to *protect the* myocardium from rapid fatty degeneration and the removal of large exudates, absorbing slowly *or containing* debris which might *contribute to* constrictive pericarditis, are often *indicated. It should be kept in mind*

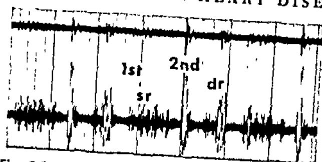


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Phonocardiography. Phonocardiography is most useful when a system which is sensitive to high-pitched vibrations (logarithmic tracings, filtered tracings using bands 100 to 300) is employed

According to Cossio's description, the typical rubs may occur in three phases· presystole, early systole, and early diastole, however, they are often found only in two phases of the cardiac cycle (Fig 8-3).

In fibrinous pericarditis, the vibrations of the characteristic systolic-diastolic *locomotive murmur* are registered According to Lian, the ordinary friction rub lasts 0 04 to 0 06 sec, with frequencies of 100 to 150 vibrations per second For comparison, a presystolic gallop usually has only 40 to 50 vibrations per second Sometimes, however, the vibrations of a friction sound may be of a low frequency also If the rub is a soft, swishing systolic sound, it may be erroneously mistaken for a "vibratory" murmur. The latter is characterized in the phonocardiogram by a regular series of vibrations of constant frequency if the tracings are taken at points distant from the point of maximal intensity (Harris and Friedman).

When an effusion subsequently appears, the friction sound progressively decreases in intensity and may finally vanish. Then, as a rule the heart sounds become weaker on auscultation. Frequently a 4th (atrial) sound can be registered in exudative pericarditis, this indicates a higher atrial pressure.

Ballistocardiography. Few ballistocardiograms of acute and subacute pericarditis have been published Winer and Zanello found bizarre patterns with marked respiratory variations in a case of pericardial tamponade.

Pneumotachography. If the oscillations of the air column in the bronchial tree are registered in exudative pericarditis by a standardized pneumotachography, the cardiopneumatic waves appear reduced in proportion to the amount of effusion, while their form and direction are maintained. Since many of the patients suffer from dyspnea or cannot hold the glottis open during respiratory standstill, the method has limited application [2]

Angiocardiography. The presence of a pericardial effusion in questionable cases can be established by this technique A distance greater than 0.5 cm exists between the contrast medium in the right atrium and the margin of the cardiac silhouette (Dotter and Steinberg). Loculated effusions and tumors can be localized and might be differentiated by combining this technique with Jansen's test. Pericardial calcification may be differentiated from myocardial calcification (Dotter and Steinberg). However, this technique should be used only with great care The patient must not be sensitive to the contrast agent, and all precautionary measures against shock, respiratory arrest, cardiac arrest, pulmonary edema, etc., must be at hand since fatalities following angiocardiography may occur

DIAGNOSIS

Since the diagnosis of a fibrinous pericarditis is based to a great extent on auscultation, it is important to distinguish a pericardial friction rub from an endocardial murmur. This is usually easy as can be seen from the comparison of murmurs shown in the following list.

[2] Pneumotachography is described in Part 4, Chap 9 *Editor*

count for an obliteration of the pericardial cavity. A child's failure to grow or hypogonadism *may be the first* sign of a constrictive pericarditis. Early *dyspnea*, disappearing at rest, slowly increasing *cyanosis*, and general *weakness* may be disregarded or misinterpreted until additional symptoms arouse attention In patients with clinical evidence of active tuberculosis, *the disease may evolve* with a multitude of signs and symptoms in the course of a few months. In patients with rheumatic heart disease, all the symptoms and signs may be erroneously attributed to the valvular lesion rather than to pericardial adhesions

Inspection and Palpation. Since accretio and concretio cordis are often combined and either may be responsible for particular symptoms or signs, they may be described together In constrictive pericarditis, inspection reveals *venous engorgement*, a *Stokes collar*, and a *protuberant abdomen* which contrasts vividly with the "stillness" prevailing over the precordium *Passive congestion* and *generalized edema* without apparent cause may be suggestive of nephritis or nephrosis. *Constrictive pericarditis* (*accretio plus concretio*) often presents a similar picture. A single vein may be compressed, producing slight cyanosis and slight edema in the respective area, or there may be swelling confined either to the lower half of the body or to the upper extremities, thus indicating different sites of venous compression. Unequal *participation of* the two halves of the chest in respiration or the involvement of a single nerve may be diagnostic clues.

In respect to the movements in the precordium, *weakness or absence of the apical impulse does not* mean a great deal The impulse may be imperceptible in normal individuals and preserved despite extensive pericardial disease On the other hand, deep adhesions located caudad *may change* the apex beat when inspiration *depresses* the diaphragm so that the apex *is neither* lifted nor thrust against the chest wall, then, even a systolic depression of the chest wall may appear However, *an increase* in stroke volume more *commonly causes* systolic chest wall depression than pericardial adhesions (Dressler)

Systolic apical retraction is a reliable sign of pericardial adhesions if (1) no positive apical impulse is visible elsewhere, (2) the retraction is brief (like a recoil), (3) the retraction remains distinct in the left lateral position, and (4) the ribs are also depressed. External as well as internal adhesions are then usually present, but only single strands, sometimes located behind the heart, may be responsible. This retraction gains *diagnostic significance* if a diastolic thrust can be proved by an electrokymogram or ballistogram and when pleural adhesions along the border of the left lung can be excluded roentgenologically. An *abrupt precordial thrust* combined with systolic retraction, a *see-saw movement*, thoracic undulation, and Brauer's thoracic shift *strongly suggest* mediastinopericarditis. The carotid impulse is of course synchronous with precordial retraction Retraction (*Hope's sign*) is most distinct when the heart is adherent to the vertebrae. A friction rub or a palpable thrill may persist despite widespread adhesions if a local fibrinous pericarditis remains active. Another pathologic thoracic pulsation is a *systolic retraction of the posterior thoracic wall* in the region of the eleventh and twelfth ribs on the left side (*Broadbent's sign*). This retraction, when present, is distinct and sometimes palpable as well and may also be noted over the false ribs on the right side, particularly when the patient leans to the left: the heart tends to sink to the left while the diaphragm pulls to the right This sign is neither common or infallible

Properly placed adhesions may produce similar retractions at the epigastrium, in the supraclavicular area, and on the anterior chest wall, particularly in the area of the lower sternum. In mediastinopericarditis, a *tracheal tug* (pulsus laryngeus descendens, *Oliver-Cardarelli's sign*) may also be felt. Diffuse *thoracic* pulsations may occur even without external pericardial adhesions (Dressler).

Certain few arterial and venous phenomena of constrictive pericarditis deserve mention. Among them is *pulsus paradoxus*· the decrease in the *height of* the arterial pulsation during *inspiration* If observed on the radial pulse, this phenomenon should not be confused with the paradoxic pulse of extrathoracic origin, due to the compression of the *subclavian artery* between the clavicle and the first rib (the latter becomes elevated during inspiration), nor with the physiologic decrease caused by collection of blood *in the* lungs in inspiration. The paradoxic pulse characteristic of adhesive

months, with repeated relapses exhausting the strength of the patient and creating special problems because of the presence of exudate. The high fever, lasting for months, makes adequate nutrition almost impossible and causes degeneration in all parenchymatous organs, particularly in the kidneys. The severe inflammatory process often extends to the neighboring organs (myocardium, pleura, mediastinum, lungs) and causes severe pain, impairs respiration, and thus initiates new complications. All these factors darken the prognosis. The exudate itself, by sheer pressure, interferes with function because it diminishes diastolic filling and hence cardiac output. Owing to this mechanical factor, sudden changes of posture may precipitate severe circulatory disturbances. The increase in intrapericardial pressure may lead to a fatal *tamponade* when surgical treatment is not employed. Severe venous stasis, intimal injury, simultaneous infection with consequent thrombosis in the systemic veins may be responsible for embolism, a complication that gravely endangers the outcome.

Still worse is the outlook for *suppurative pericarditis,* although the results have become more favorable in the antibiotic era The course and tempo of the process vary. In fulminating cases, *tamponade* may be evident by the fourth day. In unsuspected cases of pyopericardium, the only manifestation may be malaise, drowsiness, and a peculiar cyanotic pallor, until the infection becomes overwhelming. In subacute, debilitating forms of suppurative pericarditis, a generalized *secondary amyloidosis* may develop and usually indicates a fatal outcome.

It should be evident that it is impossible to make an accurate prognosis at the onset of pericarditis. With the establishment of a correct etiologic diagnosis, by consideration of the history and general condition of the patient, with the evaluation of all signs and symptoms, including the course and duration of the illness, the prognosis may be clarified However, dangerous and unforeseen complications may appear at any time

MEDICAL TREATMENT

In acute and subacute pericarditis of known bacterial etiology, the medical therapy requires the administration of the *proper antibiotic,* as well as supportive therapy. If it is possible to determine the drug sensitivity of the provocative microorganism, the most powerful drug may be prescribed. Nevertheless, it must be stressed that the most efficient antibiotic in vitro is not necessarily the most successful in vivo. While most antibiotics diffuse into the pleural and pericardial fluid, some clinicians prefer the additional *instillation of penicillin into the pericardial sac* (20,000 units in 5 to 10 ml physiologic saline solution, Hussar and Holley). However, a definite risk is present every time a pericardiocentesis is performed. Sometimes, a *specific antiserum* may be helpful (tularemia, anthrax, etc.)

In tuberculous pericarditis, whether fibrinous, serous, or purulent, the treatment should be started at once with combinations of specific drugs, irrespective of cardiac therapy. At the beginning, *streptomycin* (2 Gm daily), *isoniazid* (400 to 600 mg daily) and *para-aminosalicylic acid* (10 Gm daily) should be administered until symptomatic improvement takes place. When the temperature becomes normal, streptomycin can be reduced to 1 Gm per day, and later to twice weekly; isoniazid to 300 mg should be given daily to minimize the toxic effects of these drugs. This therapy must be maintained at least 18 months, depending on the gravity of the case (Myers and Hamburger; Shapiro et al). If mixed infections are present, additional antibiotics are needed. The necessary treatment of other tuberculous manifestations should not be neglected. In some cases of exudative tuberculous pericarditis, hydrocortisone therapy has been recommended (Ballabio and Sala). Pericardectomy should be performed at the earliest signs of constrictive pericarditis.

In hemorrhagic and purulent pericarditis, tuberculous or not, diffuse or encapsulated, when fibrin strings and flakes or necrotic material float in the pericardial exudate, *trypsin* or *streptokinase-streptodornase* (*Varidase*) may be instilled into the pericardial cavity in liquid (diluted with physiologic saline solution) or jelly form.[3] When an encapsulated pocket is inaccessible, an intramuscular injection may prove effective. This has an anti-inflammatory effect and breaks down the large

[3] This is still a controversial point. More experience is needed before accepting this method *Editor*

and 29 for expiration This sign may be explained in the same way as the mechanical paradoxic pulse: during inspiration, the heart compressed by taut strong mediastinal scars on all sides can receive only a little blood, with expiratory ascent of the diaphragm, the scars relax and the flow of blood increases.

In the abdominal wall, *dilated epigastric* veins are visible, but a "caput medusae" is uncommon. Owing to emaciation and restricted expansion of the lower chest plus a protuberant abdomen, the trunk may become "pear-shaped" The thin abdominal wall usually allows one to ascertain whether the indurated liver retains its smooth surface and round edge (chronic stasis) or is granular with a sharp border (*Pick's cirrhosis*). In the latter case, ascites may be observed Clinically, detectable enlargement of the spleen is less constant than hepatomegaly, but this does not hold true at necropsy Either disproportionate swelling of the legs in comparison to the abdomen or the reverse can be observed.

Percussion. The size of the heart in adhesive pericarditis varies, it is often enlarged on percussion but, in concretio, the cardiac area may be small While concomitant valvular lesions may influence the size and shape of cardiac dullness, pericardial adhesions alone do not cause a characteristic change in cardiac dullness unless there also is left-sided pleural scarring Normal shifting of cardiac dullness occurs with respiration (active) or with change of position (passive), although this is subject to individual variations When adhesions fix the heart to adjoining parts of the lungs, respiration may cause a shift in adhesive pericarditis On the other hand, deep inspiration and expiration, or a change of position, may cause no modification of the cardiac borders in some forms of external adhesions In simple internal adhesions (concretio), the active and passive shift of the area of dullness is often preserved. Total fixation is typical of external pericardial synechia, but a simple rigid pleural scar may also prelude cardiac motions, at least in one direction

Percussion of the lungs may reveal wide scarring with pleural adhesions Chronic stasis may cause a broad pleural scar to swell and to become edematous, so that the distinction from hydrothorax may be difficult or impossible Pleural effusions are present in nearly one-half of the patients seeking hospitalization. The effusion is usually a transudate and develops first on the right side, frequently long before the legs swell

Percussion of the abdomen may reveal a large *ascites* and, after removal of the fluid, an *enlargement of the liver and spleen.*

Auscultat[illegible] Relatively often the 2d heart sound is re[illegible] of increase[illegible] lation An[illegible] heard It occurs shortly after the 2d sound, probably when the rapid inflow into the ventricle under higher venous pressure is suddenly checked by the scar tissue. The relative frequency of this protodiastolic sound under other conditions, such as a pericardial effusion (Holldack) and in primary amyloid (Hetzel et al), remains to be determined. Since a 3d heart sound is often unusually distinct and the 2d sound is often split, phonocardiography may be necessary to interpret the data of auscultation

A soft early-diastolic murmur in decrescendo may be heard over the 2d or 3d left interspace. If the pulmonary conus is compressed by scar tissue, a *systolic thrill* and *murmur* may be found in the 2d and 3d left interspaces. Complicating valvular lesions or extracardiac compression of the mitral ostium by scar tissue may change the auscultatory findings

A *protodiastolic murmur* (the so-called "vibrance pericardique protodiastolique" of Lian) is often found with an associated pericardial calcification The murmur starts with rapid ventricular filling and may be explained as follows: a plaque of calcium, forcibly bent by systolic contraction, returns to its original position at the beginning of diastole to produce a series of diastolic vibrations Despite possible abnormal sounds, murmurs, or snaps, which may be detected in adhesive and constrictive pericarditis, in most cases auscultation reveals little (the "small quiet heart" of Beck).

Auscultation of the lungs is often negative. Over the abdomen, one occasionally hears a *perihepatic or perisplenic friction rub* indirectly caused by cardiac movements

EXTRACARDIAC FINDINGS

Polycythemia may occur, but *anemia* is more common Usually the *serum protein level* falls, and sooner or later the albumin-globulin ratio

that pericardiocentesis carries a certain risk. Often *pericardiotomy* will be necessary.

Adequate nursing and careful supervision of the diet are mandatory. If possible, the food intake should provide enough proteins and calories and abundant vitamins. Serum electrolytic studies should be made when indicated and abnormalities corrected when necessary.

The relief of pain is an important problem in the therapy of acute pericarditis. *Salicylates, phenacetin,* and related drugs (combined with *barbiturate* or *Doriden*) may give relief. *Codeine* is usually effective when pain is due to cough Not rarely, with severe pain, it becomes necessary to use *morphine* or *Demerol.*

ADHESIVE AND CONSTRICTIVE PERICARDITIS

Incidence. *Partial adherence* of the pericardium was found in 23 per cent and complete adherence in 2.226 per cent of 1,900 unselected autopsies (Sprague, Sprague et al). Adhesions may be found with extracardiac diseases such as aortic aneurysm. Precise figures on the relative incidence of accretio and concretio cordis are not available, usually they are not reported separately

Pericardial adhesions are observed at all ages, but the clinically significant varieties are encountered principally in children and young adults The syndrome is more common in *males* (Dalton et al), and in constrictive pericarditis, the ratio of sexes is practically 2:1 Although the disease is encountered in infants as well as in the aged (up to 78), about one-half of the patients are under 25 years of age Thus in 52 American patients, the age of onset was 0 to 1 year, 1, 1 to 10 years, 0, 10 to 19 years, 13; 20 to 29 years, 13, 30 to 39 years, 11, 40 to 49 years, 7, 50 to 59 years, 7 In 65 per cent of the patients, symptoms had been present for more than 2 years when relief was sought Thus, symptoms had lasted 0 to 1 year in 18, 2 to 5 years in 19, 5 to 9 years in 10, 10 to 19 years in 3, 20 to 29 years in 2

Causes. Any irritant stimulus capable of producing an acute pericarditis, from a snug plaster cast on the chest to an amebic pericarditis, may provoke pericardial adhesions The constrictive type is currently ascribed to tuberculosis (Andrews et al.), but under certain circumstances, though rarely, other factors like hemopericardium, actinomycosis, or malignancy, may cause a similar picture.

CLINICAL ASPECTS

Adhesions are the characteristic evidence of this condition. However, in certain cases, adhesions may be so thin and delicate that they do not hamper the cardiac movements at all even if they obliterate the entire pericardial cavity (*pericarditis adhesiva interna*). In other cases, dense and firm adhesions convert the thin pericardial membranes into a leathery structure, 2 to 3 cm thick, and may extend to the mediastinum or encircle the heart (*constrictive pericarditis, mediastinopericarditis*). Wenckebach compared the two extreme variants to a thin rubber glove, which permits the surgeon to execute the finest movements of the fingers, and to a boxing glove, respectively

Of course there are numerous varieties of adhesions, not only in respect to the thickness but also to the extent, location, etc., and certain descriptive names have been applied *partial or total concretio,* or *synechia,* for a partial or total fusion of the epicardium and pericardium; this may also be classified as *anterior, posterior,* or *lateral.* In *accretio cordis,* the adhesions extend from the pericardium to the pleura, diaphragm, and the chest wall At present, an attempt is made to go beyond these simplifications by exact localization and evaluation of the adhesions, so that one can obtain a better understnding of the local dynamic changes and be better prepared for a surgical intervention

SYMPTOMS AND SIGNS

Adhesions provoke symptoms and signs only under special conditions. By fixing and compressing the heart and blood vessels, adhesions may cause physiologic phenomena to disappear and pathologic phenomena to appear. Since no single symptom is constant and all symptoms may be absent despite extensive adhesions, it is scarcely surprising that this pericardial lesion so frequently escapes detection

The *history* may be uninformative. A blow on the chest in the remote past may be responsible in certain cases The interval between an infection and manifestations of constrictive pericarditis may be as short as a few months or as long as 30 years A long-forgotten, but substantial, respiratory infection may ac-

ession of the hepatic vein. This syndrome is und in tuberculosis, actinomycosis, and tu-ors The distribution of the stasis is striking. ie upper half of the body is practically free om edema, while chronic congestion makes ie hard swollen legs almost shapeless. Usu-lly *ascites is also present*. Examination of eart and lungs is negative, except for accen-uation of the 2d pulmonic sound. The respira-ory excursion of the right posteroinferior lung order is greatly reduced or absent. A strip of paravertebral dullness two to three fingers in breadth may be found above the diaphragm in the same area *Venous pressure is higher in the legs than in the arms.*

Superior Caval Syndrome. The degree of occlusion, the rapidity of its development, and the presence or absence of collateral circulation determine the clinical picture Dyspnea and cough are early symptoms, but nearly one-half of the patients have some underlying disease which might readily explain them Edema of the area drained by the superior cava is the most important sign The swelling regularly involves the face and may affect neck, arms, either one or both sides of the thorax, and sometimes the larynx Pleural effusions form in one-fourth of the patients Cyanosis sometimes develops acutely in the area drained by the superior cava *Venous pressure is higher in the arms than in the legs.* Vertigo, headache, tinnitus, drowsiness, stupor, and even unconsciousness are common

Constriction of the Pulmonary Artery An extensive rheumatic mediastinopericarditis may constrict the pulmonary artery about 2 cm above the pulmonary valve and freeze it in a normal position or displace it toward the sternum The clinical picture is that of a *supravalvular pulmonic stenosis* In contrast with this, constriction of the pulmonary veins is rather rare

Predominant constriction of the left ventricle causes a picture of pulmonary congestion and right ventricular distention which simulates mitral stenosis (White et al)

Pick's syndrome (cardiac cirrhosis) may also result from chronic hepatic congestion due to right heart failure (mitral stenosis), tricuspid defects, etc. In these cases, liver cirrhosis is due to the combination of congestion and anoxia of the liver plus an inflammatory process (perihepatitis) The patients may present all combinations and degrees of signs and symptoms, including those of severe constrictive pericarditis. In severe cases, the abdomen is distended by ascites and, after tapping, an enlarged, granular nontender liver is readily felt. The enlarged spleen is not always palpable. A "frosted" or "iced" liver is often found at necropsy, sometimes with a perisplenitis. The perihepatitis and perisplenitis may be found whenever chronic ascites of an inflammatory nature exists.

SEQUELAE AND COMPLICATIONS

Most sequelae and complications have already been mentioned. The following complications occur but are not common. Clubbed fingers and toes, elephantiasis, and hypertrophy of the male breasts are reported. Venous anastomoses provide favorable sites for the formation of thrombi. Portal thrombosis with its characteristic symptoms may occur. Dilated esophageal or hemorrhoidal veins or a retroperitoneal varix may rupture. Coronary artery changes are not unusual in constrictive pericarditis.

LABORATORY FINDINGS

Roentgenography. Simple pericardial obliteration without thickening of the membranes usually cannot be detected, in connection with pericardial adhesions, three patterns have been described: (1) a triangular shadow with straight oblique borders, (2) a globular shadow with acute left and right edges, (3) a mitral or aortic configuration (Fig. 8-5). The incidence of these types is said to be 13:8:5, respectively. This classification, however, is arbitrary, and variations (irregular contour, angular or polygonal borders, etc.) are frequent. In general the median shadow is normal or slightly enlarged, particularly in the atrial region, since the atria are relatively less constricted. The superior vena cava often dilates because of increased venous pressure Extreme enlargement of the cardiac shadow indicates a coexisting valvular lesion. Shrinking adhesions may pull the heart upward, lateral, forward, or backward. Very frequently, adhesions in the cardiodiaphragmatic angle (*bands of Stuertz*) immobilize this section of the diaphragm or produce a rhythmic systolic tug on the left diaphragm. Near the rigid adhesions, pulsations of the median shadow may

pericarditis is largest in the postexpiratory phase (Katz and Gunshot) (Fig. 8-6). The diagnostic value of this sign is not great, unless it becomes extremely obvious.

In constrictive pericarditis, *arterial pressure* is usually low (90 to 100 mm Hg systolic) and *pulse pressure* is small (15 to 25 mm Hg). *Venous pressure* may be increased three to eight times (200 to 400 mm water), this increase has few variations and does not disappear at rest. The high venous pressure and the dilatation of the veins may involve the entire body because of the "inflow stasis" or occur only in certain areas, indicating in this way the site of obstructed venous return. In place of the normal inspiratory venous collapse, an *inspiratory swelling* of the jugular veins may be noticed when anterior adhesions kink the veins or pull on the right atrium.

In adhesive and constrictive pericarditis, *circulation times* are frequently prolonged. A comparison of circulation times obtained by various methods may help to locate the site of predominant obstruction. However, more important information is gained by *catheterization* of the cavae, the *right atrium and ventricle, and the pulmonary artery* (White), and also by left heart catheterization

The *heart rate* at rest *is somewhat increased in constrictive pericarditis* (88 to 100). Unable to augment its output by larger diastole (and systole) during exercise, the heart responds to increased venous return with excessive *exertional tachycardia*. The stroke volume of the left ventricle is low and changes but little with exercise. Cyanosis may be absent or moderate or very intense, and its severity may vary with change in posture, depending upon the site of adhesions.

There are few respiratory signs of adhesive pericarditis worth mentioning Wenckebach demonstrated that retraction of the lower chest with simultaneous flattening of the abdomen may replace the normal forward movement during inspiration. This phenomenon is most obvious in profile views (Fig 8-4). Wenckebach believed that this sign indicated anteroposterior adhesions between the pericardium and the mediastinal pleura Coexistent left-sided pleural scar processes with shrinking of the left hemithorax may of course change the situation. In children with adhesive pericarditis, the spine yielding to the traction may curve, with its concavity toward the crumpled side.

Cooper's Sign. Normal subjects can hold their breath for 40 to 70 sec in inspiration and 20 to 25 sec in expiration. In myocardial failure, the figures average 25 and 15 sec, respectively. Mediastinal and pericardial adhesions are said to reverse the results. Cooper registered 9 sec on the average for inspiration

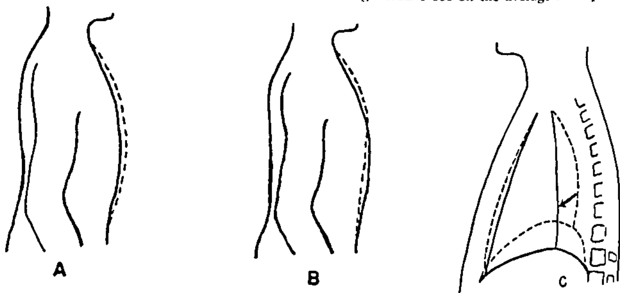


Fig. 8-4. Wenckebach's phenomenon. Respiratory profiles. dotted lines indicate inspiration. A. Normal. B Constrictive pericarditis C Compression of the heart during inspiration (unbroken line) in a case of concretio cordis with paradoxical pulse The rigidity and thickness of the anterior pericardium prevent its forward motion The scarred posterior pericardium in its forward and downward movement (arrow) on inspiration narrows and compresses the pericardial space and impairs diastolic filling.

ARTIFICIAL PNEUMOMEDIASTINUM. The induction of an artificial pneumomediastinum anterior or posterior has been recommended in order to visualize the pericardium and to demonstrate external adhesions (Condorelli). This procedure entails some dangers and has failed to gain general acceptance Flat adhesions usually can be demonstrated as individual strands by careful fluoroscopy from different angles, particularly when combined with roentgenkymography. It is especially useful in the diagnosis of accretio

Electrocardiogram. Changes in the mobility of the heart may be discovered by means of electrocardiography Upon changing from the right to the left lateral recumbent positions, the normal heart may move up to 5 cm and undergo a distinct rotation Therefore, the normal ECG shows certain changes, leads I and III and the chest leads revealing a modification of the electrical axis. When cardiac mobility is abolished by mediastinopericarditis, the ECG *recorded in the various positions may be identical* and there is no change of the axis (Dieuaide) This sign is by no means pathognomonic since extreme cardiac enlargement prevents rotation, while restriction of rotation varies according to the location and extent of adhesions

In constrictive pericarditis the ECG is frequently abnormal (Dalton, Pierson, and White) The QRS complexes show low voltage in 55 to 60 per cent of the cases, particularly in lead I. The P wave is abnormal in 72 per cent and fails to show much improvement following operation One-half of the patients show a right axis deviation. The T wave may be low in all standard leads or may be isoelectric, inverted, or diphasic in only two leads, especially in lead II With sinus rhythm, the P waves are often of normal size, but auricular fibrillation *is not* uncommon; usually it persists after operation

The electrocardiographic changes during and after operative procedures are well known and complex.

Phonocardiography. In adhesive pericarditis, phonocardiography does not reveal typical diagnostic changes of the heart sounds A few frequently recorded signs may be mentioned. (1) *Both heart sounds are decreased* but increase after successful operation (2) *The 2d pulmonic sound is usually accentuated* and larger than the 2d aortic heart sound and is often *split.* (3) Some cases develop *a large 3d sound* after operation due to increased rapid filling (Schoelmerich et al.). Phonocardiography may aid by exact timing and by establishing the frequency and duration of the vibrations in order to distinguish a pericardial protodiastolic sound from a normal 3d or 4th (atrial) sound (Evans). The pericardial protodiastolic sound is encountered almost exclusively *with pericardial calcification* and occurs about 0.1 sec after the 2d aortic sound (McKusick; Leatham).

In some cases it is difficult to differentiate by auscultation mitral stenosis from adhesive pericarditis (Luisada and Montes). In such cases, the tracing may reveal either a *late-systolic snap* or a protodiastolic snap followed by a few aftervibrations (Luisada and Alimurung)

Ballistocardiography. In simple, uncomplicated pericardial adhesion, no change of the ballistocardiogram should be expected However, constrictive pericarditis with restricted cardiac motions suggests abnormal features. In most cases, recorded in a side-to-side direction, the initial portion of the systolic complex was distorted, characteristically large and abnormally early. Mid-diastolic waves have also been found; the late diastolic waves (L, M, N, O) decrease in size. However, the specificity of these changes is doubtful (Dock et al.). After successful operation, the ballistocardiogram ordinarily reverts to normal within a few months.

Pneumocardiogram. This tracing may reveal systolic negative notches during inspiratory standstill, taut adhesions seem to be the cause Otherwise asymptomatic parietal and visceral adhesions may produce irregularities of the curve (Hochrein and Laplace).[4]

Angiocardiography. Angiocardiography may afford some help in establishing the diagnosis of constrictive pericarditis McKusick regularly found dilatation of the superior cava and sometimes mural cardiac thickening on the right side, as well as an obliteration of the *retrosternal space.* Other findings are dilatation of the pulmonary artery and a pronounced dilatation of the left atrium. Nevertheless, no localized inflow obstruction was demonstrated. This would substantiate the idea that the di-

[4] See Part 4, Chap 9. *Editor.*

is reversed. Sometimes the serum globulin is absolutely increased. Usually liver function may continue normal for some time. Even when all protein loss is balanced, the protein level drops slowly but definitely, possibly because the patient is unable to synthesize albumin (Elias and Kaunitz). With the appearance of *Pick's syndrome*, liver function is severely disturbed.

VARIETIES

Some clinical types of adhesive pericarditis may be outlined for didactic purposes:

Silent Type. The history and the physical examination during life are uninformative. At necropsy, a total internal adhesion obliterates the pericardial cavity.

Stationary Type. The illness either can be dated from a known pericarditis, or pericarditis was overlooked or was not mentioned. A careful history may recall bouts of rheumatic fever, a long-lasting tuberculosis pleuritis, a severe lung infection, a prolonged fever after confinement, or a "hilar tuberculosis" in childhood. After a long period of well-being, but sometimes without interval, symptoms develop A relatively short walk may cause severe exhaustion. Exertional dyspnea occurs, or slight cyanosis appears. Myocardial disease is suspected, but no improvement follows. Death occurs from various causes after many years of illness

Slowly Progressive Type. After months or years of relative well-being, the gradual decline occurs Contracting adhesions fix the heart more firmly, prevent diastolic filling, and hamper systole, or an old valvular lesion may progress until the precarious existence of a cardiac cripple comes to an end

Sometimes the congestion is predominant in the portal circulation, and *abdominal paracenteses* are needed The intervals between taps progressively shorten The considerable loss of protein promotes a vicious circle by diminishing the colloid-osmotic pressure; the anoxic liver is unable to build sufficient albumin, and ascites as well as general edema increase, unless revascularizing of adhesions or formation of anastomoses delays the unfavorable course for some time.

Constrictive Pericarditis. This condition is usually provoked by more or less extensive lesions of tuberculous origin (Pickering). The first symptom to appear ordinarily is exertional dyspnea, sometimes preceded by prolonged fatigue. Dyspnea occurs with or without bilateral pleural effusion, ascites, auricular fibrillation or flutter, apparently as the result of cardiac encasement and compression. The other initial symptoms in descending order of frequency are edema, enlarged abdomen, palpitation, abdominal discomfort, cough, orthopnea, vertigo, nausea, and vomiting. In the complete picture (according to different statistics), dyspnea was present in about 80 per cent, abdominal swelling in 47 to 60 per cent, hepatomegaly in 89 per cent, neck vein engorgement in 86 per cent, pleural effusion in 50 per cent of cases. Calcium deposits were noted on x-ray, operation, or necropsy in 54 to 60 per cent of cases. The heart size was either normal (46.6 per cent), or slightly enlarged or even markedly enlarged. The cardiac shape may be globular, triangle, or boot-shaped The aortic knob often is small or not visible on x-ray. Usually systolic blood pressure is normal, but the pulse pressure is often low, even 20 mm Hg. However, normal or increased blood pressure does not rule out constrictive pericarditis The circulation time is usually prolonged This results from both a myocardial factor as well as pericardial compression (Deterling and Humphreys, Harvey et al.).

Pericardial Calcification. Although not directly responsible for symptoms or for cardiac failure, calcification of the pericardium is evidence that adhesions are present. Pericardial calcification occurs in constrictive pericarditis twice as often in males as in females (Harrison and White). It has been encountered at any age In many cases, the complete absence of symptoms and signs is remarkable, so that patients were engaged in heavy work and strenuous activities. Ascites may be caused by the associated adhesive pericarditis. Auricular fibrillation (common) and flutter (unusual) may be observed. Paroxysmal tachycardia has been attributed to calcification along the sulcus longitudinalis or in the septum. Calcification of the pericardium requires no special therapy, but its presence may modify the surgical approach

Inferior Caval Syndrome. Any localized adhesions in the right diaphragmatic-mediastinal angle near the inferior vena cava may cause enormous enlargement of the liver by com-

same principles laid down for exudative pericarditis. This also holds for general care

Paracentesis of the abdomen (more rarely of the legs) may be necessary when edema is *not* controlled by diuretics. Usually symptomatic relief and lowering of venous pressure immediately follow the removal of ascites While the duration of relief becomes progressively shorter, the circulation can be maintained in this way for a long time.

The dietetic rules are easier to apply in these cases since patients are usually afebrile. On the other hand, the situation is complicated by the long duration of the disease. Skin infections, etc., must be avoided in the edematous patients as far as possible and, if already present, must be treated with antibiotics.

The only curative treatment is surgical relief from the mechanical obstruction. If successful, dramatic improvement follows.

is reversed. Sometimes the serum globulin is absolutely increased. Usually liver function may continue normal for some time. Even when all protein loss is balanced, the protein level drops slowly but definitely, possibly because the patient is unable to synthesize albumin (Elias and Kaunitz). With the appearance of *Pick's syndrome*, liver function is severely disturbed.

VARIETIES

Some clinical types of adhesive pericarditis may be outlined for didactic purposes:

Silent Type. The history and the physical examination during life are uninformative. At necropsy, a total internal adhesion obliterates the pericardial cavity.

Stationary Type. The illness either can be dated from a known pericarditis, or pericarditis was overlooked or was not mentioned. A careful history may recall bouts of rheumatic fever, a long-lasting tuberculosis pleuritis, a severe lung infection, a prolonged fever after confinement, or a "hilar tuberculosis" in childhood After a long period of well-being, but sometimes without interval, symptoms develop A relatively short walk may cause severe exhaustion. Exertional dyspnea occurs, or slight cyanosis appears Myocardial disease is suspected, but no improvement follows Death occurs from various causes after many years of illness.

Slowly Progressive Type. After months or years of relative well-being, the gradual decline occurs Contracting adhesions fix the heart more firmly, prevent diastolic filling, and hamper systole, or an old valvular lesion may progress until the precarious existence of a cardiac cripple comes to an end

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Inferior Caval Syndrome. Any localized adhesions in the right diaphragmatic-mediastinal angle near the inferior vena cava may cause enormous enlargement of the liver by com-

the azygos vein, there is an associated marked elevation of the venous pressure. A positive hepato-jugular reflux *is* also elicited which is based on a mechanism totally unrelated to the mechanism responsible for its genesis in heart failure. If this abdominal-compression maneuver is performed during the performance of the circulation time with saccharin or Decholin or calcium, the values obtained may be more markedly prolonged. This prolongation is apparently due to *the fact that* the signal substance in traveling from the arm to the right side *of the* heart moves circuitously through the inferior caval tributaries. By compressing the abdomen and thereby increasing the intra-abdominal pressure, the injected substance is halted in its route through the collateral channels for mechanical reasons (abdominal "tourniquet" effect)

HEPATIC DISEASES

The circulation time may be employed as an aid in distinguishing *congestive hepatomegaly due to heart failure from the hepatomegaly of intrinsic disease of the liver* In the latter, whether due to hypertrophic cirrhosis, metastatic disease, amyloidosis, or any other cause, the circulation time is invariably within the range of normal It will *not* be significantly affected by compression of the large liver during the performance of the test (as in superior vena cava obstruction below the azygos vein), since this compression will not interfere with the prompt emptying of the blood from the brachiocephalic portions of the body, but exercising a "tourniquet" effect, it may momentarily block the blood traveling upward from the lower portions of the body In congestive heart *failure, the* circulation time is usually prolonged, but it may also be more markedly prolonged when the abdomen is compressed, because of an entirely different mechanism which augments the venous return from the lowermost portions of the body during this compression *maneuver and thereby* causes greater dilution as well as interference with the migration of the tracer substance in its passage to the right side of the heart.

The ascites that accompanies *cirrhosis of the liver* or any other condition associated with disturbance of water metabolism may mirror closely the ascites that accompanies congestive heart failure with *or without* functional or organic disease of the tricuspid valve. Circulation time, among other diagnostic means, offers a tool for rapid differentiation *between the ascites of cardiac and noncardiac* origin In the ascites caused by cirrhosis of the liver and allied *conditions, both the arm-to-*lung time and the lung-to-tongue time are *normal, unless there is an associated anemia* (in which case it may even be reduced). On the contrary, the cardiogenic form of ascites carries with it a marked prolongation of the circulation time Readings of 12 to 18 sec for the arm-to-lung time and 25 to 50 sec (on rare occasions, 60 sec) for the arm-to-tongue time have been obtained.

RENAL DISEASES

In the anasarca of nephritis, nephrosis, *or* hypoproteinemia, the circulation time is normal, but may be reduced if there is anemia. In the edematous states that accompany congestive heart failure, both the arm-to-lung and lung-to-tongue times are invariably delayed

be small or even absent, but parts not encased by scar tissue may show particularly strong pulsations.

In *anterior adhesions (accretio)*, the retrosternal field is narrow, indistinct, and does not clear up in deep inspiration. The heart rises with the anterior chest wall instead of descending with the diaphragm during forced inspiration. Also, during swallowing, the heart and even the aortic arch may rise. Analogous conditions may be caused by posterior adhesions. If the adhesions predominate on one side (usually the right), there may be a lateral cardiac shift or the heart may assume a slightly oblique position. Such contracting adhesions may displace the esophagus by traction and subsequently may even cause esophageal diverticula (Fleischner).

Fluoroscopic tests of the passive mobility of the heart on deep inspiration or change of position in PA and lateral views are of great importance: the vertical shift of the heart is frequently impaired or even abolished. However, massive cardiac enlargement without adhesions may present the same signs Vaquez and Bordet prefer to do this examination during deep respiration in the left lateral position (in this position the heart normally moves to the left in inspiration) and, for comparison, in the upright position (the normal heart moves downward). The authors consider failure of the respective shifts as pathognomonic. Yet these and other "lesser" signs are not conclusive for they may be due to a mediastinal-pleural process, etc, without pericardial involvement. Nevertheless, when several of them are clearly present, they favor the diagnosis of constrictive pericarditis (Zdansky and Boyd).

Intrapericardial calcareous deposits may embrace the entire heart like armor, or they may be scattered over the entire cardiac surface. They are most common in the vicinity of the pericardial reflections and in the coronary grooves. Since they easily escape observation when the plaques do not lie parallel to the path of the x-rays, the examination must be made at various angles. This usually permits differentiation of pericardial calcifications from others in the myocardium, valves, pleura. Ordinarily, *calcified aortic valves* move upward and *calcified mitral valves* downward during cardiac contraction, while *calcified thrombi* in the left atrium are often ovoid. Tomography may be of great importance here, particularly for the localization of constricting strands

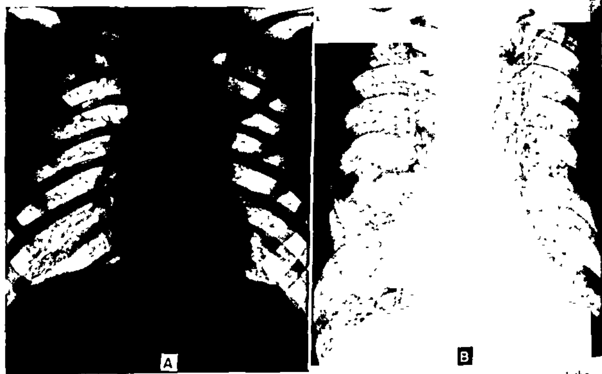


Fig. 8-5. Constrictive pericarditis. A. Globular type. Scar tissue particularly marked around the upper mediastinum. B. Triangular type. Scar tissue around cardiac borders, particularly on right side and at left base.

rhythms). The diastolic expansion of the ventricular wall is suddenly checked by the fibrotic tissue of the pericardium. Thus, the 3d *sound* easily acquires a special magnitude and a higher pitch A high-pitched *diastolic click* is recorded frequently in calcification of the pericardium and has a wide diffusion. This occurs at the time of rapid filling and again is the pathologic equivalent of a 3d sound

A typical finding is that of a *systolic click or snap*. This is a high-pitched vibration at, or after, the middle of systole, frequently followed by a few smaller vibrations (Fig. 8-6). Cases where two or three small extra sounds are present in systole may occur (Fig. 8-7). An abnormal depression or an additional wave of the cardiogram frequently coincides with the click.

PULSE TRACINGS

Simultaneous tracings of the jugular veins and of the radial pulse reveal the frequent existence of *Kussmaul's phenomenon* inspiration causes swelling of the jugular veins and simultaneous weakening (or even disappearance) of the radial pulse (*pulsus paradoxus*) (Fig. 8-8). Disappearance of the pulse during expiration, a more unusual phenomenon, is called *Riegel's sign* This phenomenon, though typical of constrictive pericarditis, may be observed to begin even in pericarditis with effusion.

PNEUMOCARDIOGRAM

An abnormal phenomenon, consisting of the inversion of the normal systolic waves, has been described in cases of constrictive pericarditis (Hochrein and Laplace). In the author's cases, on the contrary, the waves were of normal type, but *smaller* than in normal subjects. The difference in the findings may be explained by different criteria used in the selection of the cases

JUGULAR TRACINGS

It is typical to obtain tracings with poor amplitude of all waves. This is in contrast with the visible engorgement of the jugular veins.



Fig. 8-8. Paradoxical pulse Highest waves after end of expiration From above, brachial pulse; respiration (inspiration = downward movement), ECG Neoplastic pericarditis with effusion and adhesions

ameter of the venae cavae can be greatly reduced without interfering with an efficient circulation, provided that the ventricles are sound (Sellors).

DIAGNOSIS

The diagnosis of adhesive pericarditis may be relatively easy, extremely difficult, or impossible. The diagnosis depends upon a great number of symptoms and signs, the significance of which varies. None is infallible.

Constrictive pericarditis may closely simulate *cirrhosis of the liver*, but patients with constrictive pericarditis and an enlarged liver are usually younger, nonalcoholics, and have no history of vitamin-B deficiency. Portal cirrhosis is rare in infants and children Distended neck veins and paradoxic pulse are absent in hepatic cirrhosis. Changes in hepatic function are, as a rule, slight in Pick's syndrome and very definite in liver cirrhosis.

Concato's disease, strictly speaking, should present evidence of active serosal tuberculosis. Then the fluid in the peritoneal cavity is an exudate, while the ascites in chronic constrictive pericarditis is either a transudate or is border line. Moreover, transudates in the various serous cavities are often converted into exudates owing either to prolonged constant irritation or to secondary infection In polyserositis the hard, small liver is covered by a dense capsule (chronic perihepatitis), while three-fifths of the patients with constrictive pericarditis have no "frosting" on the tremendously enlarged liver It is obvious that, in *Pick's syndrome*, a double mechanism takes place, so that the liver is large, cyanotic, and "frosted"

A constricting pericardial scar compressing the pulmonary artery may evoke most of the usual phenomena of *mitral stenosis* Primary amyloidosis of the heart with stiffness of the cardiac wall may present signs similar to those of constrictive pericarditis (Gunnar et al.). The same holds for fibroelastosis.

COURSE AND PROGNOSIS

The etiology and the course of the antecedent acute and subacute pericarditis provide some clues to the course and prognosis of the subsequent adhesive pericarditis A second important element is the correct appraisal of the present lesion.

If, for example, an adult patient had rheumatic fever with a short-lasting fibrinous pericarditis many years earlier, and has been able to continue his work without any discomfort, it may be assumed that his present adhesive pericarditis, revealed by a few unimportant signs, will cause little harm. If, on the other hand, the patient had a tuberculous pericarditis and pleuritis one or two years before, never completely recovered, still has recurrent bouts of fever, and becomes dyspneic on exertion, thorough examination may reveal a constrictive pericarditis with progressive tendency which will require surgical intervention. Between these extremes, all intermediate stages may occur and may make a correct prediction difficult.

The ultimate outcome of rheumatic adhesive pericarditis is poor when the process starts during the period of active growth (3 to 8 years); the recurrent attacks and the development of adhesions may initiate a train of slowly progressive, unfavorable symptoms It is uncommon for a child with an old rheumatic endocarditis and clinically obvious adhesive pericarditis to live more than 3 years However, most deaths are caused by the valvular and myocardial lesions rather than by the pericardial adhesions. Terminal bacterial endocarditis, bronchopneumonia, or a severe attack of acute rheumatic fever may hasten the end. In rare cases of constrictive pericarditis, no symptoms are present in spite of unequivocal compression, in these cases, life expectancy does not seem altered. Sometimes constrictive pericarditis may last for years, during which time the patient remains more or less an invalid in spite of energetic medical treatment.

[illegible]

alone offers a real prospect for rehabilitation. However, operative and postoperative deaths (pulmonary edema, pulmonary embolism) are still not uncommon

MEDICAL TREATMENT

Existing adhesions cannot be influenced by medical therapy, but an effort may be made to help the damaged circulation, to relieve stasis, and to improve the condition of the heart muscle. In general, therapy follows the

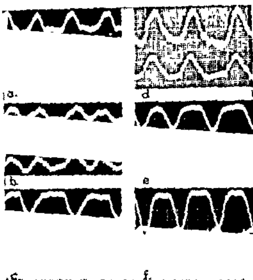


Fig 8-10 Electrokymograms at selected points of the cardiac silhouette. Upper curve is the EKy; lower curve is the pulse wave of the carotid artery. *a.* Ascending aorta *b* Spicule of calcium at the root of the aorta *c.* Midportion of right border showing plateau-like curve *d* Pulmonary artery *e and f* Middle and lower portions of the left border, showing plateau-like curve Note wave on carotid pulse coincident with onset of diastolic plateau of the EKy (From Gillick Radiol 1950)

commencing very shortly after the beginning of diastole and ending with the onset of systole The mechanical restriction also produces an interference with the characteristic secondary waves of both isometric contraction and isometric relaxation The descending or emptying component of the wave has about the same duration and angle as the ascending or filling limb The overall appearance of several cycles is that of a *straight line with V-like interruptions* constituting the emptying and filling components. Several reports showing this type of wave in chronic constrictive pericarditis have been made in the literature McKusick refers to these waves at "flat-tops and V's" (Fig 8-9)

Electrokymograms of patients with clinically diagnosed and surgically proved chronic constrictive pericarditis have been shown by several investigators to have these characteristic waves Figures 8-10 and 8-11 are roentgenograms and EKys, respectively, of a patient having an obvious constrictive pericarditis with marked calcification which was demonstrated at a later date by surgery. On the EKys, the lower curve is a recording of the carotid pulse—it should be noted that a wave occurs on the carotid graph at the onset of the plateau, *i e.*, at the point where diastolic filling is abruptly terminated. This wave occurs approximately at the time of occurrence of the "3d heart sound" frequently described in such patients. This is probably a reflected wave produced by a phenomena similar to the water-hammer effect.

With adequate surgery, the restrictive effect of the diseased pericardium is removed partially or wholly. This release is followed at once by a more adequate ventricular filling, which is reflected by the postoperative EKy of ventricular motion. McKusick shows a particularly illustrative case of the marked change in the ventricular EKy (Fig 8-11).

The so-called "flat-top" with the "V emptying and filling component" is *not* necessarily pathognomonic of constrictive pericarditis. However, the existence of such a wave form together with other evidence compatible with the diagnosis of chronic constrictive pericarditis can usually be considered evidence that

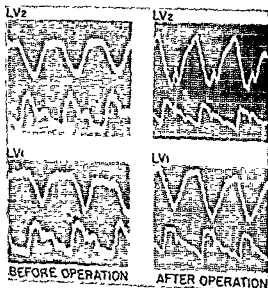


Fig. 8-11. Typical flat-top and V pattern of chronic constrictive pericarditis on left before surgery On right, the EKy has returned to normal postoperatively. Note "reflected wave" on carotid pulse in preoperative graphs; it is absent or markedly diminished in postoperative tracing. (*Proc. First Conference on Electrokymography. P.H.S. Publ. No.* 59.)

4

Circulation times in pericardial diseases

WILLIAM M. HITZIG

CONSTRICTIVE PERICARDITIS AND PERICARDIAL EFFUSION

In these two conditions (extracardiac only in the sense that there is no severe involvement of the myocardium), the venous pressure may be high, because of cardiac compression by scar tissue in the former and fluid pressure in the latter The circulation times in these instances may mimic those which are obtained in right heart failure. In *constrictive pericarditis with predominant compression of the right heart,* the arm-to-lung time may be increased On the other hand, it may be entirely normal There are rare instances of constrictive pericarditis in which the compression *involves predominantly the mitral ring,* and then the circulatory dynamics closely mimic those of mitral stenosis In such instances (depending upon the degree of myocardial fatigue involving the right heart), the ether time may be within normal limits while the lung-to-tongue time is considerably prolonged as in mitral block

In *pericardial effusion,* the compression invariably involves the right side of the heart, although selective compression of cardiac chambers may also occur. When the venous pressure reaches high proportions (it must exceed intrapericardial pressure to be compatible with life), either the ether time or the arm-to-lung time is often considerably elevated. On the other hand, the lung-to-tongue time, except for rare instances of dominant left ventricular compression, remains within normal limits.

Constrictive pericarditis may cause a picture which closely resembles that of congestive heart failure as seen in diseases that affect the left side of the heart. When that occurs, the differential diagnosis cannot be made on the basis of circulation time alone.

SUPERIOR VENA CAVA OBSTRUCTION

Engorgement of the veins of the brachiocephalic portions of the body due to either a mediastinal tumor or thrombosis of the superior vena cava may be differentiated by means of circulation-time tests. A high venous pressure, if accompanied by superficial thoracic varicosities under venous tension, indicates that the obstruction of the superior vena cava is below the azygos vein; the arm-to-lung time will be increased to a range between 10 to 14 sec, or it remains within the upper limits of normal. This may be due to passing of ether through the collaterals of the inferior vena cava en route to the right heart and the lungs. The arm-to-tongue time may be prolonged, but obviously the lung-to-tongue time will remain within the normal range. The circulation time, executed from the femoral vein (thigh-to-lung time and thigh-to-tongue time) with ether and Decholin, will give normal readings (4 to 8 sec for the former and 10 to 16 sec for the latter).

Of interest is the fact that, when the obstruction of the superior vena cava is below

7

Surgical treatment of constrictive pericarditis

J. GORDON SCANNELL

The surgical treatment of chronic constrictive pericarditis is an example of the logical evolution of a clinical idea The consequences of constrictive adhesions of the pericardium were described by Chevers (1842). He concluded that "the principal cause of dangerous symptoms (in scarring of the pericardium) appears to arise from the occurrence of gradual contraction in the layer of adhesive matter which has been deposited around the heart, compressing its *muscular* tissue and embarrassing its systolic and diastolic *movements*, but more particularly the latter"

[illegible]

colleagues Brauer (1902) proposed "cardiolysis," meaning resection of the rigid precordial structures without actual liberation of the constricting encasement of the heart Although Brauer's operation appears inadequate and illogical in the light of subsequent knowledge, it served the purpose of stimulating further attempts to correct the mechanical problems created by the disease Rehn (1913) first resected a constricting pericardium with benefit to his patient. The operation was first carried out in this country by Churchill (1928) The operative relief of chronic constrictive pericarditis has now become an accepted surgical procedure

Although, as we have seen, the hemodynamics of constrictive pericarditis were well described in 1842, for a full century thereafter the problem of *inflow stasis* was debated. Constriction of the venae cavae and right atrium was often thought to be the cause of the marked peripheral venous hypertension that is so characteristic of this disease. All direct evidence, however, particularly that obtained by cardiac catheterization, supports the view that inflow stasis is the result of encasement of the ventricles and interference with their function, particularly diastolic filling, rather than encroachment upon the right atrium and orifices of the great veins Burwell and his associates (1951) reported cardiac catheterization studies of patients with constrictive pericarditis and concluded that *individuals who have an elevated peripheral venous pressure associated with pericardial disease can be assumed to have a degree of congestion in the lungs similar to that which exists in the periphery.* Their evidence, which has been confirmed on many occasions, suggests that the function of both the right and left ventricles is seriously impaired, thus reaffirming the need to focus the surgical effort on liberating these structures rather than decorticating the atria and great veins.

A source of confusion is the failure to distinguish between adhesive and constrictive pericarditis The former, which frequently follows rheumatic pericarditis and consists of avascular adhesions obliterating the pericardial sac, is of little clinical significance. Even calcification and thickening of the pericardium itself are of little consequence as long as the

Graphic data in pericarditis

ALDO A. LUISADA

PHONOCARDIOGRAM

In *dry pericarditis*, the *friction rubs* are represented on the sound tracing by vibrations of various pitches, with those of higher pitch prevailing. These vibrations are grouped in either two or three phases of the cardiac cycle The most common are those which occur during presystole and systole (to-and-fro rubs), the latter being louder (Fig 8-3); a third group may take place in early diastole (Cossio). The systolic rub is due to friction of the pericardium during ventricular contraction, the presystolic rub is caused by friction of the pericardium during atrial contraction, the early diastolic rub is caused by friction of the pericardium during rapid ventricular filling and is the least loud on account of the slower motion causing it.

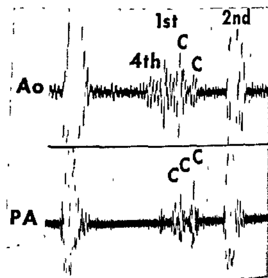


Fig. 8-7. Filtered phonocardiograms at aortic and pulmonic areas Unusual case of multiple pericardial adhesions with multiple clicks (C, C, C).

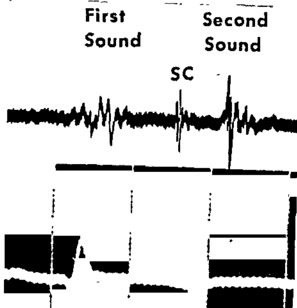


Fig. 8-6. Phonocardiogram (stethoscopic) at apex. Systolic click (SC) due to apical pericardial adhesion. (*From Luisada. Heart Beat,* 1953).

Increased compression with the microphone increases the loudness of the vibrations, probably through modification of the acoustic properties of the microphone. The vibrations of the rubs are more easily recognized when no endocardial murmurs are present.

In *constrictive pericarditis*, it is possible to note increased loudness of the *2d pulmonic sound* This is evidence of constriction of the left cardiac chambers followed by higher pressure in the pulmonary circulation.

A *triple rhythm* of either the atrial or ventricular type is frequently recorded (see Part 3, Chap 9, for detailed description of these

of cardiac constriction or embarrassment is present, this should not be persisted in beyond a few weeks. *Digitalis* is indicated if some degree of myocardial damage is suspected, and also in older patients (i.e., over 50 years of age) who are considered candidates for operation. Salt restriction is wise, although this should not be carried to the point of electrolyte depletion, particularly in the patient who is about to undergo an operation which will of itself tend to lead to further salt depletion. Mercurial diuretics, ammonium chloride, and other diuretics may be used if the patient is carrying an unusually large fluid load, but ordinarily will be of limited effectiveness. A daily record of weight is a useful method of following the patient's fluid balance during the preoperative period.

SURGICAL TECHNIQUE

General anesthesia is necessary for adequate pericardiectomy. The terms pericardiectomy, pericardiolysis, and decortication are used interchangeably. The important point is that adequate amounts of scarred, constricting pericardium be removed from the heart to permit free and unhampered diastolic filling of both ventricles.

Choice of incision lies between a *left anterolateral thoracotomy* and a *vertical midline sternotomy*. Bilateral anterior thoracotomy has been advocated, and although this incision is extremely useful in a number of situations, particularly where open cardiotomy is contemplated, it carries the disadvantage of bilateral pleural complications and discomfort to the patient without being necessary for adequate exposure of the heart in constrictive pericarditis.

Although a median sternotomy is easier to make and to close than a left anterolateral intercostal incision, and although it provides excellent access to the right ventricle and atrium and the venae cavae, it does not allow the ease of approach to the left ventricle and the left AV groove which is provided by a left anterolateral thoracotomy. Since complete liberation of both ventricles is the major objective of operation, in the author's opinion a left anterolateral approach is the method of choice. This is usually carried out in the 4th intercostal space, and the pleural cavity is opened widely.

The intercostal incision should be carried anteriorly to the edge of the sternum after isolation and division of the internal mammary artery and vein. The medial surface of the left lung is freed from the surface of the pericardium, and the phrenic nerve is identified and carefully spared after dissecting it free from the level of the hilum to the diaphragm. The anterior surface of the pericardium can usually be easily freed from the undersurface of the sternum.

Once the external aspect of the pericardial sac has been well defined, a cruciate incision is made through the pericardium at a site estimated to be to the left of the anterior descending coronary artery. The incision is carried through all layers of the pericardium down to the soft, flexible epicardium. Once this plane has been established, the pericardium is carefully dissected from the surface of the heart. In the performance of this dissection, there is little danger of penetrating the wall of the relatively thick-walled ventricles, but there is considerable hazard of wounding major coronary vessels as they course over the surface of the heart, and these may give rise to troublesome bleeding. If they are damaged, the bleeding should be controlled by very fine sutures of No. 00000 arterial silk. Areas of calcification, particularly those which appear to penetrate the myocardium, are particular points of hazard, and small islands of calcification may be left upon the heart without prejudicing the effect of operation. It is especially wise to do so if the islands of dense calcification lie in the groove of the anterior descending coronary vessels.

The pericardium should be removed from the left ventricle first. The resection should be carried back to the entrance of the left pulmonary veins into the left atrium just above the left AV groove. This will be posterior to the original site of the phrenic nerve as it lay on the external surface of the pericardium; hence it is important to identify and spare that structure early in the operation. Usually, the tip of the left auricle will be easily demonstrated, and it is ordinarily not necessary to carry the superior dissection further. The pericardium should then be removed from the posterior surface of the left ventricle and down over the apex. The operator's attention is then focused on the right ventricle, and similar flaps of pericardium are removed from this chamber. Although the anterior surface of the pericardium lies beneath the sternum, it can be brought into the operative field by traction. The latter may cause some dislocation of the heart, with consequent embarrassment to its

Electrokymography in pericarditis and constrictive pericarditis

FREDERICK G. GILLICK

The *intrinsic* motions of the heart, its changes in density, and its positional motions are summated in stimulating the photoelectric components of the electrokymograph (Part 4, Chap. 8). The relative weights of each component are difficult to determine in any given record but would appear to be in the order named. With involvement of the pericardium and the pericardial "space," changes in the recordings obtained by the EKy will be primarily related to the damping effect on the primary intrinsic motion or action of the heart —this may be of a definitive restrictive character or of a masking type.

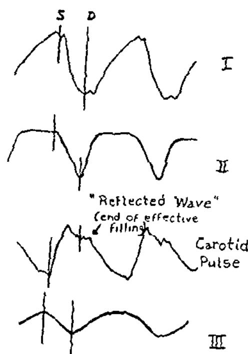


Fig. 8-9. I. Normal ventricular EKy. II. Ventricular EKy in chronic constrictive pericarditis with definite restriction of diastolic filling. III. Ventricular EKy in pericardial effusion.

In pericardial involvement there is a range of effects so far as the EKy is concerned. An *acute pericarditis* without a radiologically apparent amount of effusion usually produces *no* characteristic changes. With a frank radiologically apparent effusion, the EKy produced from the ventricular borders *eliminates most, if not all, of the secondary waves* associated with isometric contraction and relaxation and the valve closures involved. An undulating type of wave with few, if any, secondary waves is recorded. This curve is not necessarily characteristic of an effusion per se, as it is merely a recording of a dense mass oscillating as it were across the "slot" of the EKy synchronously with the cardiac cycle (Fig 8-9).

Until the pathologic process of *chronic constrictive pericarditis* produces changes sufficient to offer resistance to complete filling, the ventricular curve may be quite "normal" in appearance, or it may have a number of unexplained sharp, peaked secondary waves superimposed on a grossly normal basic curve. With effective restriction of ventricular filling, several characteristics of the ventricular curve develop. These characteristics are a reflection of an *abrupt halting of the diastolic filling process* by mechanical restriction of the lateral motion of the ventricle—thus produces a plateau

8

Pathologic aspects of myocarditis

OTTO SAPHIR AND ALBERT I. RUBENSTONE

In the past, the designation "chronic myocarditis" was applied without distinction by clinicians to virtually every disease of the heart muscle. In the majority of instances, the actual underlying disease process was replacement fibrosis resulting from coronary arteriosclerosis. After pathologists succeeded in inculcating clinicians with the desirability of limiting the term to primary inflammation of the myocardium, the diagnosis of myocarditis was seldom made except in the presence of rheumatic fever or as a complication of diphtheria. Interest in the clinical recognition of myocarditis has been revived in the past 15 years as the result of the stimulus of careful morphologic, electrocardiographic, and clinical studies. Today, myocarditis is accepted as a common complication of a variety of infectious diseases, at times dominating the clinical picture and determining the ultimate outcome of the illness.

INCIDENCE

Estimates of the incidence of myocarditis are at best an approximation, because of the difficulty which clinician and pathologist alike experience in establishing the diagnosis. The diagnosis may be overlooked by the practicing physician because of an unawareness of the clinical entity of myocarditis.

The pathologist may overlook the diagnosis because of failure to take an adequate number of sections from the myocardium, since myocarditis is frequently focal as well as diffuse. In over 6,000 autopsies performed in a large general hospital, the incidence varied from 4.3 to 9 per cent (Saphir, 1942). The higher incidence was encountered when larger numbers of sections were taken from the heart. The incidence was higher in children than in adults, doubtless as the result of a relatively larger mass of heart muscle examined for the same number of histologic sections. An incidence of approximately 3.5 per cent was reported from the Armed Forces Institute of Pathology from among 40,000 autopsies (Gore and Saphir, 1947). De la Chapelle and Kossman reported an incidence of myocarditis in 3.3 per cent of 1,250 consecutive autopsies at a general hospital and an incidence of 7.8 per cent in a review of 1,000 autopsies performed at a contagious disease hospital. Marcuse found 36 instances of nonspecific myocarditis among 3,800 autopsies in 1947, and Blankenhorn and Gall reported an incidence of myocarditis of 2.5 per cent from the study of 3,194 autopsies during the period from 1949 to 1953.

CLASSIFICATION

A classification of myocarditis which is not overlapping and serves both the pathologist and the clinician is difficult. A primarily etiologic classification, while not entirely satisfactory to the pathologist, has the advantage of usefulness from the standpoint of the clinician. Accordingly, the subject may be presented under the following categories.

Myocarditis due to known infectious agents.

1. More commonly associated with endocarditis and caused by: (a) bacteria, such as staphylococci, streptococci, pneumococci, gonococci, and meningococci, and very rarely by B. anthracis, *Klebsiella pneumoniae* (Friedlander's bacillus), salmonellae, brucella organisms, pseudomonas, *Hemophilus influenzae*, and *H. parainfluenzae*. Also rarely the tubercle bacillus may cause both endocarditis and myo-

the pathologic condition is restricting effective diastolic filling. Tachycardia or an associated significant pleural effusion may on the other hand mask the "flat-top and V" pattern.

Other conditions can mimic this curve, such as a marked bradycardia as is seen in complete AV block. This occurs because there is a normal limit to diastolic filling time, and when this limit is reached, the lateral movement of the ventricular border ceases. *Extrapericardial disease* could also conceivably limit lateral motion of the cardiac border, thus producing a plateau-type curve during a portion of the diastole.

8

Pathologic aspects of myocarditis

OTTO SAPHIR AND ALBERT L. RUBENSTONE

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process does not cause contracture of the pericardium.

There is considerable evidence that tuberculous infection of the pericardium commonly, if not regularly, progresses to chronic constrictive pericarditis (Andrews, Pickering, and Sellors), although it is usually impossible to demonstrate tubercles in the resected specimen following pericardiectomy. Antecedent trauma, pyogenic infection, and hemopericardium have at all times been implicated, with good circumstantial evidence.

DIAGNOSIS AND INDICATIONS FOR OPERATION

The diagnosis of chronic constrictive pericarditis may be obscured by associated evidence of liver and intrinsic heart disease In general, the diagnosis should be suspected when there are signs of intractable right heart failure in the absence of valvular heart disease, particularly if the heart is small. Roentgenographic demonstration of calcification of the pericardium is an important clue, but as has been pointed out above, it does not establish the diagnosis of constrictive disease Although the most common picture is that of the small, quiet heart, moderate degrees of cardiac enlargement are not infrequent

The symptoms and signs of constrictive pericarditis are those of peripheral venous hypertension plus pulmonary congestion Dyspnea is a common complaint. Dependent edema, hepatomegaly, and ascites are usually prominent The heart sounds may be muffled, but are not necessarily so, and a distinct 3d heart sound may be heard A *paradoxical pulse* is commonly present and though not necessarily diagnostic of pericardial disease —either constriction or compression—is one of its most striking signs [1]

From the surgical point of view, one feature of the electrocardiographic findings deserves special emphasis. The presence of *atrial fibrillation bears an ominous prognosis*, perhaps because it signifies an unfortunate degree of myocardial involvement It does not constitute, however, a contraindication to operation.

Operation is indicated in constrictive pericarditis if it can be reasonbly shown that the patient is suffering from a constricting pericardial process and *not* from myocardial failure or degeneration. In the younger patient, particularly in the absence of active myocarditis, this is usually relatively easy to do. In the older patient, it may be more difficult, requiring a period of medical therapy, which generally has only limited success in the patient with constrictive pericarditis. Such patients respond poorly to diuretics and only fairly well to salt restriction and digitalis. If considerable myocardial involvement is present in addition to the pericardial disease, the success of adequate surgical operation is proportionally limited. Worthwhile alleviation of symptoms may be achieved, however

The timing of operation is an important consideration. Before effective chemo- and antibiotic therapy for tuberculosis was available, operation was reserved to the quiescent, or chronic, phase of the pericardial disease. Operation was, however, recommended during the subacute phase if the patient had reached a plateau of improvement or was actually deteriorating under supportive therapy. Operation during the acute phase of pericardial effusion was, and even now ordinarily is, contraindicated if the patient is making a satisfactory response to medical therapy. The risk of disseminated tuberculosis is now greatly reduced, and operations may be undertaken early in the course of pericarditis if it seems reasonably certain that the disease is progressing to constriction. As mentioned earlier, this ordinarily excludes rheumatic pericarditis and the majority of nonspecific pericardial effusions. Should operation be undertaken when considerable effusion persists, it is important, and in fact easier, to perform as liberal a decortication as would be done in the presence of a dense and relatively avascular pericarditis. Adequate antibiotic and chemotherapeutic coverage of such patients is important.

PREOPERATIVE PREPARATION

The preoperative preparation of patients with constrictive pericarditis follows, in general, the regimen of all patients undergoing cardiac operations. A suitable period of supportive therapy and medical observation is mandatory. If the diagnosis of tuberculosis has been established or strongly suspected, a period of antituberculous chemotherapy is indicated, but if the evidence for some degree

[1] See Chap. 3.

tis, *Aschoff bodies* may also be demonstrable in a surprisingly large percentage of cases. While the older literature mentions circumscribed areas of inflammation (the so-called *Bracht-Wachter bodies*) *in the myocardium*, it is generally considered that there is no clear-cut single histologic entity to which such a term could justifiably be assigned. On the other hand, *minute infarcts* in various stages of organization are often found in the myocardium in acute and subacute bacterial endocarditis. These infarcts are the result of broken-up bits of vegetations forming emboli in coronary artery branches.

While all organisms which produce endocarditis often also cause *myocarditis*, there are many instances of myocarditis caused by these agents in the absence of endocarditis. Thus, organisms of any bacteremia and pyemia may lodge in the myocardium. *Gonococcic* and *meningococcic* myocarditides occur in the absence of endocarditis. *Focal necrosis* with abscesses and the presence of the organisms have been found in gonococcal myocarditis. The organisms have also been demonstrated in the myocardium in meningococcic myocarditis. Hemorrhages into the skin and suprarenal glands (*Waterhouse-Friderichsen syndrome*) have been found in association with meningococcic myocarditis.

In *brucellosis*, myocarditis with or without endocarditis may occur. Granulomatous lesions have been found in the myocardium, consisting of histiocytes, lymphocytes, plasma cells,



Fig. 8-12 A. Myocarditis with abscess secondary to generalized pyemia. Note bacteria in center of abscess. B. Myocarditis associated with bronchopneumonia. C. Myocarditis due to mycotic infection (*Aspergillus*). D. Myocarditis in rheumatoid arthritis.

function and arrhythmias. Should these occur, it is well to relax traction or pressure on the heart and allow it to recover its equilibrium. The *surface application of local anesthetics is of little effect.*

As resection of the pericardium proceeds, the increased diastolic filling of the heart becomes immediately apparent in the operative field. This may be accompanied by a corresponding widening of pulse pressure and an increase in the systolic pressure. Although there should be relatively little major bleeding during the course of the dissection, there may be considerable slow blood loss from the many adhesions that must be divided. Blood loss should be replaced by transfusion.

At the conclusion of the dissection, the operative field should be dry and the incision may then be closed with intercostal catheter drainage of the left pleural cavity. The latter drainage tube is left in place on suction for approximately 48 hr.

The remainder of the postoperative care resembles that of any major thoracotomy. Particular care is necessary to help the patient rid himself of bronchial and tracheal secretions. Adequate blood and fluid replacement are important, avoiding excessive replacement but at the same time being aware of the problems of salt depletion If digitalis was given preoperatively, it is continued postoperatively If the patient was in regular rhythm preoperatively, he is usually given protection doses of quinidine, i e , 0 2 Gm every 6 hr, postoperatively, for 4 to 5 days. Careful record of fluid intake and output are essential.

RESULTS OF OPERATION

In the absence of severe myocardial damage, an excellent result can be expected to follow adequate pericardiectomy in almost all cases of constrictive pericarditis Unfortunately, a number of these patients have complicating myocardial disease, and the differential diagnosis of progressive cardiac failure versus recurrence or residual pericardial disease may be most difficult It is probably true that recurrence of symptoms and signs is not the result of re-formation of scar over the heart but rather the result of progressive constriction of pericardium which was left at the time of the original pericardiectomy. Hence, it is important to excise as much pericardium as possible from the ventricles at the initial procedure, particularly posteriorly and in the region of the left AV groove. In a number of reoperations, the author has found this a particularly likely site of residual constricting pericardium, with the previous operative field uniformly obliterated by adhesions of a nonconstricting type. The source of recurrent difficulty is found in residual scarred pericardium, unless the cause lies within the heart itself.

Reoperation is governed by the same principles as an original operation, with the added technical difficulty of taking down old operative adhesions. It can generally be adequately accomplished through a left anterolateral thoracotomy. If further exposure is needed, this can be obtained by extending the incision medially across the lower end of the sternum, or laterally farther out in the interspace.

The beneficial effects of operation may be apparent early in the convalescent period but may not become obvious for several months Maximum improvement should be reached 4 to 8 months from the time of operation. The decision to reoperate is not an easy one, but should be made if the patient fails to show the expected degree of improvement from the original operation and there is (1) doubt as to the adequacy of the original pericardial resection, (2) evidence by cardiac catheterization of persistent constricting scar, and (3) no clear evidence, electrocardiographically, of intrinsic heart disease. The data of cardiac catheterization alluded to will be the presence of the characteristic early-diastolic dip and plateau (or square-root sign configuration) of the right ventricular pressure curve, and the presence of mild persistent pulmonary hypertension with a low fixed cardiac output. The latter, of course, may be equally well present with some degree of left ventricular failure, and the decision to reoperate will always be the result of careful weighing of the clinical and laboratory evidence.[2]

[2] In doubtful cases, left heart catheterization should be performed. *Editor.*

ingly impossible in so-called acquired syphilitic myocarditis, using the various present-day methods available for staining.

Mycotic infections may involve both the endocar[illegible] and the myocardium, or either alone. T[illegible] scesses[illegible] in these lesions culturally and often also [illegible]torially in the histologic sections. Thus, blastomyces, torula, actinomyces, monilia, histoplasma, and coccidioides may be demonstrable. It seems that, since the advent of antibiotics, *fungus infections* have been encountered more frequently than before. The authors have found candida and aspergillus abscesses in the myocardium of patients who have been treated for minor infections with antibiotics (Fig 8-12C).

Protozoal Infestations. These are usually confined to the myocardium, affecting neither the endo- nor the pericardium. Since the myocardium is always secondarily affected, it is important to look for other manifestations of the disease, although cardiac lesions may be of major importance. Myocarditis in these instances is not necessarily due to the actual localization of the parasite within the myocardium but may be the result of an *allergic reaction* toward the various protozoa or parasites, or may signify the reaction toward necrotic myocardial fibers, the etiologic agent being no longer demonstrable.

The myocardium may on rare occasions disclose an amebic abscess, the pericardium being usually first affected because of a *ruptured* amebic liver abscess.

South American *trypanosomiasis* (*Chagas' disease*) caused by *Trypanosoma cruzi*, affects principally the myocardium (Decourt et al.; Romano) and the central nervous system. In the heart, the organisms localize within the myocardial fibers which rupture, and myocarditis ensues. Often such a myocarditis is widespread and causes death. An interesting fact is that within the circulating blood the parasite is present in the form of a trypanosoma, but on entering the myocardial fiber, it changes to a leishmanial form. While parasitization of the fibers is not accompanied by inflammatory changes, inflammation ensues after rupture of the fiber has occurred. Myocarditis is characterized grossly by a dilated, soft, and flabby myocardium. There is often a complicating pericarditis. Microscopically, the inflammatory exudate consists of lymphocytes, plasma cells, eosinophils, macrophages, and also a few polymorphonuclear leucocytes. Thus myocarditis often becomes chronic.

Myocardial changes may occur in all forms [illegible]. These changes are usually degen[illegible] ber of capillaries in the myocardium [illegible] filled with parasitized red blood corpuscles, plugging the lumens of these vessels. Interstitial edema, foci of hemorrhages, and degenerative changes of muscle fibers result. Very rarely, true interstitial myocarditis has been described.

Myocardial involvement is common in *toxoplasma* infections. Next to the central nervous system, the commonest site of the infection is the myocardium, involving the muscle fibers themselves. Foci of necrosis and infiltrations of polymorphonuclear leucocytes, eosinophils, and monocytes are occasionally observed. However, it seems that the organisms are also able to invade muscle fibers without causing necrosis and without provoking an inflammatory reaction.

Among *helminthic infections*, the most important one is *trichinosis*. Trichinous myocarditis is a serious and often fatal complication. While the larva does not encyst in the heart, in passing through the myocardium or remaining there, it produces myocarditis of various degrees of severity. Microscopically, the inflammatory exudate consists of polymorphonuclear leucocytes, lymphocytes, macrophages, and often large numbers of eosinophils. Foci of necrosis of muscle fibers are almost constant. Also small foci of extravasated red blood corpuscles may be noted. The larvae are rarely found in the necrotic foci.

Other parasitic diseases rarely cause myocarditis. However, since a number of parasites in various forms of development sometimes pass through the heart or myocardium, changes may occur which may cause either a nonspecific myocarditis or, as Jaffé postulated, an allergic (hyperergic) inflammation.

Also, in rare instances of *schistosomiasis*, the larval worm or ova may be deposited in the myocardium and cause myocarditis.

Myocarditis in Virus Diseases. Myocarditis seems a rather common complication of virus diseases. Although clinical evidence may be

carditis. (*b*) *Mycotic infections,* such as brought about by blastomyces, candida (monilia), actinomyces, histoplasma, coccidioidomyces, etc.

2. Usually *not* associated with endocarditis: (*a*) Klebs-Loeffler infections; (*b*) protozoal *infections (amebiasis, trypanosomiasis,* especially the South American form of Chagas' disease, and very rare instances of leishmaniasis, malaria, and toxoplasmosis); (*c*) helminthic infections, especilly trichinosis and, more rarely, *schistosomiasis;* (*d*) *rickettsial diseases* (typhus, scrub typhus, Rocky Mountain spotted fever), (*e*) viral diseases and diseases most likely caused by viruses. (Included here are influenzal A and B infections, measles, mumps, *infectious mononucleosis, poliomyelitis,* encephalomyocarditis, yellow fever, epidemic viral hepatitis, varicella and variola, Guillain–Barré syndrome, pertussis, and Coxsackie virus infections).

Myocarditis associated with diseases of obscure etiology, such as occurs in rheumatic fever, rheumatoid arthritis, collagen diseases (Libman-Sacks disease, disseminated lupus erythematosus, dermatomyositis, scleroderma, periarteritis nodosa), Friedreich's ataxia, hemorrhagic fever, and Boeck's sarcoid Also belonging in this group is myocarditis associated with glomerulonephritis, uremia, or pregnancy.

Myocarditis as a primary isolated disease entity (isolated or Fiedler's myocarditis).

Myocarditis due to chemicals, either as a direct result or due to hypersensitivity ("allergic," "hyperergic" myocarditis, such as reactions to antibiotics, sulfonamide, or serum), this group includes cases due to quinidine, carbon monoxide, digitalis, and potassium

GENERAL ASPECTS

The gross findings in the hearts of patients who succomb to myocarditis complicating *acute infections* may show little, if any, characteristic changes.

The heart is dilated with flattened papillary muscles and columnae carneae, of a faint yellowish gray hue, and softer than normal Microscopically, insignificant changes, or none at all, may be noted in a few routine sections Myocarditis may not be demonstrated by the pathologist, because of insufficient histologic studies To avoid such errors, a large number of sections must be cut from the myocardium and carefully examined. Diffuse myocarditis may be encountered in one tissue block cut from the myocardium, while others show no evidence of inflammation In other instances, the myocarditis may disclose a predominantly serous exudate with few inflammatory cells which may be easily overlooked. Isolated necrosis of individual muscle fibers with a minimum of monocytic cells, a finding characteristic of certain virus myocardi-tides, may also readily escape detection.

There are, of course, instances where the involvement of the myocardium is diffuse and is easily recognized. This is particularly seen in so-called "isolated" myocarditis. The *inflammatory exudate* may be located principally in the interstitial tissue (so-called *interstitial myocarditis*), or there may be severe *degenerative changes* of the muscle fibers, sometimes culminating in necrosis with resulting secondary invasion of the dead fibers by inflammatory cells (so-called *parenchymatous myocarditis*). There is no special location of the exudate. Sometimes it may be found principally in the conducting system, for example, in a few instances of myocarditis associated with viral hepatitis, the exudate has been noted particularly in the left bundle branch, in the vicinity of grossly recognized subendocardial hemorrhages (Saphir, 1956).

MYOCARDITIS DUE TO KNOWN INFECTIOUS AGENTS

Myocarditis is an important complication of all infectious diseases which are associated with the various types of endocarditis (see also rheumatic, rheumatoid endocarditis, etc). In *acute bacterial endocarditis* and *subacute bacterial endocarditis* (endocarditis lenta), myocarditis is a common complication Appreciation of this is of particular importance because, while the acute infectious disease and its accompanying endocarditis may be beneficially influenced by antibiotics, the late effects of the myocarditis may nevertheless lead to serious consequences It is incorrect to view rheumatic endocarditis as the only type which is often complicated by myocarditis.

Microscopically, the myocarditis in these instances may be more or less localized in the form of *foci of necrosis* or *abscesses* (Fig. 8-12A), or it may be diffuse, consisting principally of interstitial infiltrations of polymorphonuclear leucocytes. In bacterial endocardi-

no other major disease is found which is known to cause myocarditis, it would seem reasonable to expect that the myocarditis is also of viral origin. *In one instance*, the virus of poliomyelitis has actually been isolated from the heart.

Grossly, the flabbiness of the heart, the grayish color, and the fact that the architecture of the myocardium is obscured, i.e., that the individual muscle bundles do not appear as single clear-cut units, *are characteristic* of the myocarditis. In viral hepatitis, subendocardial *hemorrhages in* the region of the left bundle of His are sometimes seen grossly.

Microscopically, in all these myocarditides, lymphocytes and polymorphonuclear leucocytes predominate in the inflammatory exudate (Fig. 8-13A, B). Quite characteristic are necroses of individual muscle fibers, recognized either within the inflammatory exudate *or in the midst of seemingly normal* muscle fibers. In early *instances of myocarditis in* poliomyelitis, the authors were particularly impressed with the seeming outpouring of neutrophilic leucocytes. In myocarditis of viral hepatitis, a large number of neutrophils have been noted *close to the regions* of subendocardial hemorrhages.

Myocarditis also occurs in *infectious mononucleosis*, although the viral nature of this disease remains unestablished.

Extremely interesting are reports on *congenital myocarditis* brought about by the occurrence of Coxsackie B virus infections of the mother.

Myocarditis in Rickettsial Diseases. Among rickettsial diseases, myocarditis seems to occur especially in scrub typhus, epidemic typhus, and Rocky Mountain spotted fever. In the mild *form, it occurs in about 40 to 50* per cent of cases, but *is more severe in scrub typhus* and epidemic typhus. Grossly, small foci of recent hemorrhages are often seen, while microscopically, perivascular infiltrations of mononuclear cells, plasma cells, and occasional lymphocytes *and polymorphonuclear* cells with vesicular nuclei and *swollen lining endothelial* cells are seen. Recent thrombi may be present.

MYOCARDITIS ASSOCIATED WITH DISEASES OF UNKNOWN OR OBSCURE ETIOLOGY

Rheumatic Fever. In *spite of the wealth* of valuable studies and pertinent *experiments*, the cause of rheumatic fever is still obscure. Is it caused by a special type of immune reaction toward a specific organism? Is it *somehow* connected with a product *of certain streptococci*, or is it perhaps caused *by an at-present* undiscovered agent? As *has been* stated repeatedly, only the one who will be able to reproduce the most characteristic *single* granuloma within the myocardium pathognomonic of the disease—an unequivocal Aschoff nodule—will solve the riddle of rheumatic fever.

In acute rheumatic fever, endocarditis, myocarditis, and pericarditis may be present. As in other instances, myocarditis *is often difficult* to diagnose grossly. *The dilatation of the* heart with *flattening of the papillary muscles and columnae carneae* may be *clearly noted.* Multiple whitish *streaks speak* for early fibrosis and signify *later stages of* myocarditis.

Microscopically, a number of changes may be noted. First and foremost are the *Aschoff nodules*. These are not found in every instance but are almost always detectable in children dying *from acute rheumatic fever.* The authors are convinced that the frequency with which they are found is in direct proportion to the number of sections examined. This is not the place to describe the details of the Aschoff body (see Part 7). It should be mentioned that it is located in the interstitial tissue perivascularly and undergoes various changes, the *granulomatous stage being its most characteristic* form. Evidence of *fibrinoid degeneration* is usually seen. The nodule consists of several types of cells, among which the *Anitschkow cell*, or myocardial reticulocyte (also called *Aschoff cell*) is very common. Its nucleus is elliptical with chromatin fibers which resemble *the body* of a spider. On cross section the nucleus appears "owl-eyed." Also a few polymorphonuclear leucocytes and plasma cells are present. In addition, there are a few multinucleated giant cells *showing* slight basophilic cytoplasm and overlapping *nuclei*. Most characteristically, the cells are arranged in parallel rows, coursing *concentricly* about a central *blood vessel*.

In addition to Aschoff *bodies*, *there also is* degeneration and localized necrosis *of muscle* fibers, about which a few inflammatory *cells* accumulate, many of them of the Anitschkow *type*. Also, a few giant cells may be seen, *some being obviously* myogenic in origin. Such le-

and a few eosinophils. Myocarditis has been reported in *Brucella melitensis* as well as in *B. suis* and *B. abortus*.

In the various *salmonella* infections, a complicating myocarditis is rare and histologically is not characteristic. Cloudy swelling and severe fatty degeneration of the myocardium, however, are common.

Myocarditis complicating the bacterial *pneumonias* is more common than is generally appreciated. It occurs principally when large areas of lung tissues are involved and when there is evidence of early organization of the pulmonary exudate (Fig. 8-12B).

Upper respiratory infections, even *tonsillitis*, may lead to myocarditis. Myocarditis is not rare in association with *acute laryngotracheobronchitis* and is, of course, more commonly seen in children and infants than in adults. Microscopically, the myocarditis is principally interstitial, and the inflammatory infiltrate is largely composed of lymphocytes Some instances of finding infants dead in their cribs which were attributed to suffocation can sometimes be explained by acute myocarditis following unrecognized tracheobronchitis.

Myocarditis in *tuberculosis* may be the result of a mixed infection or may actually be caused by the *Mycobacterium tuberculosis*. *Miliary tubercles* may be found in the myocardium in generalized miliary tuberculosis This condition is relatively more common in children. Larger tubercles (conglomerate tubercles) are seldom found

Nonspecific lesions are also found in the myocardium which are said to resemble Aschoff bodies and which have led to speculation as to a possible causative relationship between rheumatic fever and tuberculosis However, the similarity of such lesions to Aschoff bodies has been seriously questioned and is, as yet, unverified Besides, it certainly is not impossible that a patient may occasionally have both diseases, i e, tuberculosis and rheumatic fever.

Because of the fact that tubercles are most commonly isolated minute nodules, clinical symptoms of myocarditis are practically nil Only in rare instances, when the interventricular system or the region of the nodes are affected with resulting changes in the conduction system, may subjective or objective signs of cardiac involvement be elicited.

Myocardial changes in *diphtheria*, brought about by the products of the *Corynebacterium diphtheriae*, have in the past often constituted the fatal complication of the disease. Today, with early precautionary measures and early diagnosis, diphtheritic myocarditis is relatively rare. While the disease is usually called diphtheritic myocarditis, it should be noted that the toxin produces primary *parenchymatous degeneration with necrosis* and that the exudative process (the inflammation) is a secondary reaction to the necrosis, and actually represents a reparative process. Grossly, the heart is dilated, soft, and pale, with indistinct yellowish streaks throughout the myocardium *Microscopically*, degeneration and large areas of necrosis are common, with histiocytes, plasma cells, and lymphocytes. Often, hardly discernible ghosts of muscle elements are still seen in the regions of the cellular exudate. In later stages, scars are found which over a considerable length of time still show lymphocytic infiltrations.

The Myocardium in Syphilis. While the myocardium is often involved in syphilitic aortitis as the result of narrowing of the mouths of one or both coronary orifices, true syphilitic myocarditis, the direct result of the lodging of the *Treponema pallidum*, seems extremely rare, if it exists at all. There is an extensive literature on this subject, and only a very small minority of investigators claim the existence of true syphilitic myocarditis. They describe the clinical evidence and quote isolated cases. Most of these reports originate from the southern regions of the United States, where syphilis is more common than in the northern sector. Since most reports are based on clinical observations alone, it must be emphasized that a patient may have syphilis and, in addition, also myocarditis due to other causes (*myocarditis in a patient with syphilis need not necessarily be of syphilitic origin*). In older syphilitics, myocardial ischemia with various scars is common These are the result of the encroachment upon the mouths of the coronary arteries. Gummas have been described in the myocardium. However, they are extremely rare. In congenital syphilis, miliary gummas and true inflammatory changes are found in the myocardium. These changes are rarely encountered today, and if present, it is not difficult to demonstrate *Treponema pallidum* in the microscopic sections This demonstration is seem-

carditis, occur in instances of uremia from any cause These are fatty changes, cloudy swelling, and edema. Sometimes the exudate of uremic pericarditis may extend into the adjacent myocardium. Changes similar to those occurring in *acute and subacute* glomerulonephritis may be found in the myocardium when uremia is caused by these diseases Also, myocardial degeneration and even outspoken myocarditis may be incident to the accompanied hyperpotassemia, and perhaps also to hypocalcemia.

While the *term "pregnancy myocarditis"* is *sometimes* used, *there is no special type of myocarditis incident to pregnancy per se.* If myocarditis is present, it is the result of associated diseases In instances of *toxemia of pregnancy*, myocardial changes similar to those seen in acute or subacute glomerulonephritis may occur. Also, *foci of muscle fiber necrosis have been described*

Boeck's sarcoid may also involve the myocardium Although rare, fulminating cases have been described in which the myocardial changes were thought to have been responsible for the death of the patient On gross inspection, *the heart may appear normal or may actually disclose many small grayish-white* discrete areas a few millimeters in diameter. Mi-

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lymphocytes One or two giant cells of the Langhans type *may* be present in the center of the granuloma Some of these giant cells may contain *Schaumann's or asteroid bodies* There is no necrosis A gradual transformation into hyalinized connective tissue is found in older nodules It is sometimes ventured that some *instances of* the granulomatous variety of isolated, or Fiedler's, *myocarditis might* rather be Boeck's sarcoid From a description of this type of myocarditis (see below) this seems rather far-fetched

Isolated, or Fiedler's, Myocarditis. This type of myocarditis is of unknown origin and is not accompanied by *endocarditis* or pericarditis, it occurs in patients who have no other disease that may be correlated with the myocarditis Clinically, this myocarditis may have a fulminating course, ending fatally in a relatively short time, or the clinical course may be protracted with remissions *and* exacerbations, however, ultimately it terminates *in* death. Nothing is known about the cause of the myocarditis, though various organisms, such as a special type of streptococcus or a virus, have been held responsible at various times. While it is known that certain chemical compounds, whether directly or by causing hypersensitivity, may occasionally provoke myocarditis (which is "isolated" in the sense that neither the pericardium or the *endocardium* is involved), such a myocarditis should not be classified as isolated in the sense of Fiedler's myocarditis but rather as "hyperergic" or "chemical," etc. Also, myocarditis caused by *vitamin deficiency* or as seen in certain instances of *endocrine disturbances* must not be classified as isolated myocarditis. It is conceded that, as more is learned about various causes of the *myocarditides and the agents which* produce them, *the less frequent* the diagnosis of "isolated" myocarditis will be made.

Grossly, the heart is usually enlarged, often considerably so. It is dilated and soft except in cases of long duration, where areas of fibrosis are numerous. The heart is pale gray, yellow tinged, *often disclosing fine white gray* streaks. Microscopically, *two varieties can be* distinguished, a more diffuse type and a granulomatous form. The former is principally an *interstitial myocarditis* with lymphocytes, a few polymorphonuclear leucocytes, occasional Anitschkow cells, and large monocytes. Outspoken macrophages and fibroblasts are *not rare, and transitions* from the inflammatory exudate to early scar tissue *are often seen.* The exudate is located almost *exclusively in the* interstitial tissue (Fig. 8-13C). The *granulomatous variety* consists of smaller or larger areas where the muscle fibers are destroyed and replaced by infiltrations of lymphocytes, *monocytic* cells, and a few endothelial leucocytes, with *a sprinkling of multinucleated* giant cells. These are either muscle *giant cells* (and may represent attempts at muscle fiber *regeneration*) or are of the foreign-body type. Such areas may also be circumscribed Since outspoken true granulomas are not always present while *multinucleated* giant cells are common, the term "giant *cell myocarditis*" seems appropriate. Evidence of *necrosis of* muscle fibers is usually also noted. This variety at *some time* was thought to have been caused by *either* tuberculosis or syphilis, but this was never



Fig. 8-13. A Viral myocarditis Note necrosis of muscle fibers. B Myocarditis associated with poliomyelitis C Isolated myocarditis Note lack of necrosis of individual muscle fibers

insignificant, electrocardiographic changes have been reported in many instances, and pertinent autopsy findings are not unusual It has been observed in *measles*, although rarely, and more commonly in *mumps*, at least to judge from the electrocardiographic findings (15.4 per cent, Rosenberg). It occurs in *viral influenzal infections, Coxsackie B virus infections, viral hepatitis,* and in some instances of *interstitial pneumonitis* Although degenerative changes in the myocardium are common in *yellow fever,* myocarditis was also observed. Among seven fatal cases of *epidemic (viral) hepatitis,* myocarditis was found four times. In fatal cases of *smallpox (variola)*, inflammatory changes have been described. This is also true in *varicella.* Among eight patients who had varicella, at the time of death, myocarditis was found in all. Two of these eight patients, however, also had diphtheria.

Interesting and of clinical importance are neurotrophic viruses which apparently also produce myocarditis. As a matter of fact, the *encephalomyocarditis virus* was so designated because of its ability to produce, in the experimental animal, at least, both encephalitis and myocarditis. There are also reports of patients with both diseases, presumably caused by the encephalomyocarditis virus.

In two of these patients, an agent could be demonstrated in the blood serum which was neutralized by the serum of patients who had recovered from the disease. These patients may have outspoken clinical evidence of encephalitis, and later develop electrocardiographic changes and tachycardia, etc, succumbing rather quickly, or may present a fulminating clinical picture with fever and convulsion, and die unexpectedly.

More common is the myocarditis of *poliomyelitis.* While autopsy statistics do not give a true picture of its incidence, it has been reported in about 40 to 50 per cent of cases.

Interesting is the study showing that, when only routine sections were cut from the heart, myocarditis was encountered in 16 out of 92 cases, but where multiple sections of the heart were available, myocarditis was present in 45 of these same 92 cases More important, however, for the overall picture, is the clinical incidence Thus, of 62 children with poliomyelitis more recently observed, 21 showed electrocardiographic changes. During epidemics, the incidence of myocarditis is much greater than otherwise.

In all these instances, *the virus origin is, of course, only presumptive* and must remain so until the virus can actually be demonstrated in the myocardium However, if the virus nature of the primary disease is established and

old myocardial changes incident to embolic phenomena [2]

Isolated, or Fiedler's, myocarditis not rarely becomes chronic Such patients develop gradually more and more severe myocardial failure, with a relentless downhill course of months and even years, until they succumb with severe congestive heart failure. The term *pernicious myocarditis* was coined to indicate the unmerciful course of the disease

Chronic myocarditis always causes considerable enlargement of the heart It is possible that numerous episodes of cardiac dilatation contribute to the hypertrophy Thin whitish streaks of fibrosis are often noted Microscopically, the myocardium on low-power examination may look like a sieve, with meshes which constitute small areas of fibrosis and only a lattice of hypertrophic muscle fibers A few inflammatory cells are often recognized in the fibrotic regions, in at least some of the sections. So-called *idiopathic hypertrophy of the heart*, as seen in both children and adults, may be a late result of chronic myocarditis. In chil-

[illegible]

age group The authors have seen an occasional patient past 60 years of age dying from what was clinically interpreted as coronary arteriosclerosis with old myocardial infarcts. In some of these cases there was only a minimal coronary arteriosclerosis but most severe true chronic myocarditis. While, as stated, not many years ago "chronic myocarditis" was commonly incorrectly diagnosed in patients of the older age group in lieu of coronary artery disease with myocardial damage, we have learned that, though rarely, true chronic myocarditis also occurs in this age group and is not always an error of diagnosis or terminology.

[2] See Chap 1 Editor

sions have been named *myofiber Aschoff bodies* (Murphy), but they are not specific and are really not related to true Aschoff bodies, which are always located in the interstitial tissue. In addition, a more diffuse interstitial myocarditis occurs with infiltrating lymphocytes and a few polymorphonuclear leucocytes. This type is particularly common in children and young adults.

From the above, it is clear that isolated Aschoff bodies are probably of no clinical significance since there are located in the interstitial tissue and are only found here and there. More important is the diffuse interstitial inflammation, caused by pressure of the exudate upon the adjacent muscle fibers, and the muscle necrosis. It is also evident that inflammatory changes in the vicinity of the bundle of His and of the AV node, with edema (*serous myocarditis*) or degenerative changes of these structures, are responsible for changes in the AV conduction

All these lesions eventually heal with scar formation. Most characteristic is the resulting perivascular fibrosis.

Rheumatoid Arthritis. Myocardial changes in *rheumatoid arthritis* are quite characteristic (Fig 8-12D). These changes are often adjacent to those of the valvular endocardium but may be seen at a distance from them. There may be focal collections of lymphocytes and plasma cells. However, more significant are smaller or larger areas of necrosis, in which a distinct reticular network is still faintly recognizable. At the border of such areas is a zone of inflammatory cells consisting of mainly monocytic cells (somewhat resembling epithelioid cells), which are large, radially directed, with pale staining nuclei, and which often assume a palisade arrangement These changes resemble closely those seen in the affected joints.

Myocardial Changes in Collagen Diseases (Libman-Sacks Disease, Lupus Erythematosus, Dermatomyositis, and Scleroderma). It is well known that a special type of endocarditis (atypical verrucous endocarditis of Libman-Sacks) occurs in a number of cases of *lupus erythematosus.*[1] Microscopically, a few characteristic changes are found in the myocardium in instances of lupus erythematosus, which may or may not be associated with this type of endocarditis and which may also be seen in endocarditides in the absence of outspoken lupus. Alterations in the collagen of the myocardium occur, with the fibers appearing swollen and densely stained with eosin. Arterioles and venules may be filled with platelet thrombi as in thrombotic thrombocytopenic purpura. Fibrinoid degeneration of the wall of the small arteries may be present. Outspoken focal myocarditis occurs in regions where there is a fresher fibrinoid degeneration or necrosis. Fine scars throughout the myocardium and increased density of the collagen are characteristic of older cases.

In *dermatomyositis,* edema with a varying number of lymphocytes and a few polymorphonuclear leucocytes has been found in the interstitial tissue of the myocardium. There is also proliferation of fibroblasts, with eventual new formation of connective tissue.

In *scleroderma,* there is a gradual transformation of atrophic and degenerated muscle fibers by new connective tissue. This occurs in patches and may be accompanied by a small number of inflammatory cells, principally eosinophils.

Myocarditis also occurs in *Friedreich's ataxia* and in the *Landry-Guillain-Barré syndrome.* Interstitial and diffuse myocarditis has been observed in the former, with eventual fibrosis. Mild focal myocarditis, characterized by perivascular infiltrations of lymphocytes, macrophages, and Anitschkow cells, is found in patients with the Landry-Guillain-Barré syndrome.

In fatal cases of *hemorrhagic fever,* myocarditis seems to play an important role in addition to the kidney changes.

Myocarditis Associated with Glomerulonephritis, Uremia, or Pregnancy. While some of the myocardial changes in these conditions may well be attributed to accompanying electrolyte changes or associated acute, though clinically seemingly insignificant, infectious diseases, it is usually considered that their cause is obscure. Myocarditis is not rare in acute and subacute glomerulonephritis, occurring in about 10 per cent of autopsy cases The myocarditis is principally of the serous type, with only scattered inflammatory cells and especially Anitschkow cells.

In addition to pericarditis, myocardial degenerative changes, but only rarely true myo-

[1] See Part 16, Chap. 3. *Editor.*

the patient later in life still remain virtually unexplored. It remains for future work to provide answers to these and other important questions in order that physicians may view this type of heart disease in its proper perspective in the field of cardiovascular dysfunction.

INCIDENCE

Despite the numerous statistical reports by pathologists and clinicians, the actual incidence of myocarditis is not accurately reflected in the figures of any available study. The data of pathologists suggest that the overall incidence of myocarditis is 3 to 4 per cent when routine autopsy technique is employed, but approximates 10 per cent when numerous blocks are taken from the myocardium for histologic examination. However, in interpreting such estimates, it must be kept in mind that the low mortality in most infectious diseases makes available to the pathologist only a small percentage of the total number of cases. These fatal cases, obviously, do not constitute a representative sampling of the particular disease. On the other hand, reports of the incidence of myocarditis based upon clinical grounds are unsatisfactory because of the variety of criteria which are regarded as adequate indications of myocardial involvement. Many of the signs and symptoms attributed to myocarditis are not infrequently due to hypotension, hyperpyrexia, shifts in pH, or alterations of serum electrolytes, occurring in association with the primary disease. It is not surprising, therefore, that the diagnosis of myocarditis, based solely on clinical evidence, has been reported as infrequently as 0.02 per cent and, at the other extreme, as often as 55 per cent.

The clinical incidence of myocarditis also varies with the frequency with which serial electrocardiography, utilizing multiple precordial leads, is employed during the course of acute diseases. Important in this regard, too, is the skill with which other cardiac as well as extracardiac abnormalities of the ECG are differentiated from those due to myocarditis. There are few reports available in which such electrocardiographic studies have been carried out in conjunction with careful correlation with clinical criteria. Even at best, dissociation between signs and symptoms, electrocardiographic abnormalities, and anatomic findings is frequent. For these reasons, no attempt will be made to present statistics concerning the incidence of the various etiologic types of myocarditis.

CLINICAL FEATURES

Symptoms. There is no well-defined clinical picture of myocarditis if one excludes textbook descriptions of rheumatic and diphtheritic myocarditis. Aside from the complaints attributable to the appearance of congestive heart failure, *there are no symptoms during the course of an infectious disease which are pathognomonic of myocarditis.* Precordial pain or oppression, weakness, and palpitation accompany infectious disease more often in the absence of acute myocarditis than when this complication is present. The appearance of these same symptoms, however, following recovery from an acute infection, or the occurrence of persistent asthenia or dyspnea on effort should arouse suspicion as to the presence of a postinfectious myocarditis. Occasionally, the precordial pain may be indistinguishable from that of coronary heart disease, and in its severity, it may even mimic coronary occlusion. Postinfectious neurocirculatory asthenia may be differentiated from myocarditis by careful evaluation of the patient's symptoms and emotional patterns and the absence of both signs of heart disease and abnormalities of the ECG. When heart failure complicates myocarditis, the symptoms are no different from those due to heart failure from any other cause; dyspnea and orthopnea occur with greatest regularity. Complete absence of symptoms, despite the presence of an active myocarditis, is not infrequent.

There may often be an interval of one to several weeks between the occurrence of the original infection and the appearance of signs of myocarditis. This is particularly true of respiratory infections. Many instances of preceding infection in cases of myocarditis are uncovered only through painstaking questioning of the patient. Often a patient may fail to volunteer such information because the preceding acute infection had been so trivial that no importance was attached to it. A patient with unexplained heart failure may omit mention of a previous upper respiratory infection because he sees no relation between such illness and his present heart disease. The common occurrence of such latent periods has

verified. Also, as stated above, it was more recently considered as possible evidence of Boeck's sarcoid.

CHEMICALS, DRUGS, AND POISONS WHICH PRODUCE MYOCARDIAL CHANGES

Some of the myocardial lesions are due to direct action of chemicals upon the myocardium, while others are caused by a mechanism of hypersensitivity (*allergic myocarditis*). Foremost among the latter, are those caused by the administration of sulfonamides. Changes have also been reported following administration of arsenicals, bismuth, penicillin, quinidine sulfate, ergotamine, epinephrine, atropine, emetine, and chloroform. In hypersensitivity myocarditis, the inflammatory exudate may show a preponderance of eosinophilic cells. Periarteritic changes may also be present. However, in most of the other instances, degenerative changes with only a few inflammatory changes are encountered This is also true in the experiments with various drugs given in large doses for cardiac disorders. Thus, *digitalis* and *quinidine* may also produce degenerative changes.

Well known are the myocardial changes which occur in *potassium deficiency* Degeneration, necrosis of muscle fibers, and infiltration of polymorphonuclear leucocytes are found in the myocardium

Myocardial changes occur often in illuminating gas poisoning (*carbon monoxide poisoning*). The principal changes are hemorrhages, foci of necrosis, and polymorphonuclear leucocytic infiltration Some of these lesions resemble those seen in diphtheria These changes are found, of course, only after the patient has at first survived, and have been reported in deaths occurring about 2 weeks after exposure The fact that patients may survive the original exposure but may develop evidence of myocarditis sometime later is of clinical importance

COMPLICATIONS OF MYOCARDITIS

From the foregoing, it is clear that true myocarditis is important, not only from a casuistic and morphologic point of view but also because of its clinical implications. The practicing physician is often so occupied by the severity of a primary infectious or contagious disease that he may overlook the possibility that the patient may also have myocarditis This is common in the case of patients with acute poliomyelitis.

Complications of myocarditis have received little attention. Of course, acute myocardial failure is a feared complication in every case of myocarditis. Cardiovascular collapse may ensue. Embolic phenomena are not uncommon and may be found in the pulmonary artery branches and in the coronary and cerebral arteries. The source of these emboli are apparently *small thrombi of the mural endocardium*, although this cannot be verified in every instance. The thrombi are the result of acute inflammatory changes of portions of the myocardium located close to the endocardium An insignificant mural and localized endocarditis may well be responsible for the mural thrombi.

Unexpected and sudden death is not rare in myocarditis. It is especially common in children with seemingly insignificant upper respiratory tract infections who succumb suddenly to the complicating myocarditis.

It is easily conceivable that a number of acute myocarditides may heal with complete restitution This is especially so since the inflammatory exudate in many instances is located in the interstitial spaces, leaving the muscle fibers more or less intact. However, the exudate, especially its serous component, may be so extensive that death, often unexpected, may ensue during the acute stage. There are also cases where the acute myocarditis gradually becomes subacute and eventually chronic. True *chronic myocarditis* is not rare. Chronic myocarditis may occasionally follow the various acute myocarditides mentioned above. A well-known fact is that myocarditis in Chagas' disease often becomes chronic and constitutes a common cause of myocardial failure in regions where the parasite is endemic. In some patients myocardial incompetence can be traced to myocarditis which developed in the wake of scarlet fever or other infectious diseases The complicating myocarditis is sometimes recognized clinically during the acute stage, and the patients recover only to be readmitted on later occasions because of myocardial failure, to which they finally succumb. Likewise, patients with bacterial endocarditis seemingly cured with antibiotics may eventually die in myocardial failure brought about by chronic myocarditis or

to some extent in the presence of true protodiastolic gallop rhythm, even though overt signs of heart failure may be lacking. The absence of demonstrable enlargement should suggest another basis for the gallop rhythm. This will most frequently be found to be a *summation type* resulting from the coincidence of the sound caused by atrial contraction with the 3d heart sound as a conse-

tachycardia is present, a *presystolic murmur* or the *opening snap* of mitral stenosis may be mistaken for a triple (gallop) rhythm. Usually, if attention is paid to other concomitant auscultatory signs, the differentiation is not difficult.

CONGESTIVE HEART FAILURE. Congestive failure appearing during the course of an acute infection in a patient without preexisting heart disease is indicative of acute myocarditis. Moreover, whenever cardiomegaly is encountered, with or without signs of congestive heart failure, the absence of evidence of valvular or congenital lesions, hypertension, coronary artery disease, or pericarditis should suggest the possibility of diffuse myocardial disease. Such circumstances should stimulate a search for a history of recent infection or exposure to sensitizing agents. Temperature elevation of more than 2°F rarely occurs in uncomplicated heart failure. If other causes can be excluded, the presence of such fever may provide a clue to the presence of myocarditis. The widespread tendency of diagnosing heart failure without establishing an etiology is to be deplored. Likewise, the presumption that unexplained heart failure after the age of 40 equals coronary disease must be tempered by the knowledge that pathologic studies have demonstrated the presence of 50 to 80 per cent of all cases of nonrheumatic myocarditis in just this age group (de la Chapelle and Kossmann, Saphir).

The precipitation of heart failure by infection in patients with organic heart disease poses a difficult and often clinically insoluble problem. Such a complication is commonplace in the absence of myocarditis, and yet some additional form of heart disease has been found in one report in almost 40 per cent of their cases of myocarditis (Blankenhorn and Gall).

Intractable heart failure is a common feature of so-called "isolated" myocarditis, the chronic myocarditis of Chagas' disease, and the myocarditis associated with active or healed bacterial endocarditis.

CARDIAC MURMURS. Murmurs are audible over the precordium in the vast majority of cases of acute or chronic myocarditis at some time during the course of the disease. Usually the murmur is *systolic* in time and *apical* in location. Although all variations of intensity and duration are encountered, pansystolic murmurs of high pitch are the rule. Appearance of the murmur may coincide with the onset of congestive failure. In other instances, the murmur may disappear during a bout of heart failure and return when compensation is restored. A systolic murmur may be present only while there is fever or anemia. The murmurs of myocarditis per se disappear when total recovery takes place.

Diastolic murmurs *at the apex* of the heart in nonrheumatic myocarditis are more common than is generally appreciated. Such apical diastolic murmurs occur as a result of eddy currents produced by the "relative mitral stenosis" associated with dilatation of the left ventricle. Reports of such findings in postinfectious myocarditis would be more frequent if it were not part of accepted medical dictum to place the label of rheumatic heart disease upon all patients exhibiting this kind of murmur. Cases of chronic myocarditis with such auscultatory findings may masquerade for years as rheumatic mitral stenosis only to have the autopsy disclose no evidence of valve deformity (Silber and Shaffer). Absence of a rheumatic history, of an accentuated apical 1st heart sound, and of an opening snap of the mitral valve should lead the clinician to question chronic rheumatic endocarditis as the basis for this murmur. The wide area of audibility of the murmur of relative mitral stenosis contrasting sharply with the limited area in organic mitral stenosis is also a helpful clue. In the *majority* of instances, recognition of the functional nature of the murmur is possible with phonocardiography (Luisada et al.). In those cases where doubt is still present, the differentiation of organic from functional stenosis can be made by recording the diastolic pressure gradient across the mitral valve

Clinical and laboratory aspects of myocarditis

EARL N. SILBER

Involvement of the myocardium by an inflammatory process, focal or diffuse, occurs in a wide variety of infectious diseases. Similar lesions may also be encountered in allergic reactions, the "collagen" disorders, and a number of other diseases of obscure etiology Such cardiac damage is usually disclosed by anatomic or electrocardiographic studies in the absence of clinical evidence of myocarditis. In many instances, however, subtle or obvious signs of myocardial impairment are present. Thus, acute, subacute, and chronic types of myocarditis are recognizable from both the clinician's and the pathologist's point of view

Before 1900, the scope of the term "myocarditis" was a reflection of the view expressed by Virchow and Rokitansky that cardiac fibrosis was due to previous inflammation. As a result, practicing physicians of this period designated almost every disease of the heart muscle as "chronic myocarditis" After Herrick's report (1912) of the significance of coronary occlusion, the pendulum swung to the other extreme. During the 1920s and 1930s, as physicians gained an understanding of the relationships of coronary insufficiency to replacement fibrosis of the myocardium, such strong objections were raised to the term "myocarditis" that it fell into disrepute Few clinicians made such a diagnosis except in the presence of rheumatic fever or diphtheria. Christian has been notable among those who, nevertheless, persisted in emphasizing primary myocardial disease as an important etiologic agent in many instances of heart failure. Pathologic studies of the past 15 years have substantiated this stand by demonstrating that myocarditis is not uncommon at postmortem examination (Saphir).

Although such reports have stimulated renewed interest in the clinical aspects of myocarditis, our present knowledge of the subject remains incomplete and confused. There is, in particular, a great need for studies which correlate the clinical, the electrocardiographic, and the anatomic findings in a far greater detail than has heretofore been the case There are still too many reports of "nonspecific," "idiopathic," or "isolated" myocarditis in the literature unaccompanied by serious efforts to identify an etiologic agent through the facilities of the modern diagnostic laboratory.

The development of new techniques for the isolation of viruses has produced an incredible emergence of new viruses and provided unlimited opportunity for reexamining the unsolved diseases of man. *There is already sufficient evidence to suggest that well-known, as well as the newer, respiratory viruses are far more significant agents of heart disease than has been previously appreciated.*

The importance of *hypersensitive drug reactions* as etiologic factors can, at present, only be surmised from the scattered reports of myocarditis due to various medications, antiserums, or antibiotics.

The problem of chronicity and the impact which the acute myocar[illegible] may have on

be difficult. This distinction is most reliably made radiologically by inspection of the lung fields: a large quiet heart in the presence of virtually normal lung fields speaks for pericardial effusion, a large quiet heart with lung fields which demonstrate vascular congestion favors cardiac dilatation

In the presence of murmurs and heart failure of uncertain etiology, the demonstration of valve calcifications is often of considerable value in arriving at a judgment of valvular versus primary myocardial disease. Such calcifications may be visualized by simple fluoroscopy or by the Bucky-Potter grid technique. The most accurate method, however, is by use of body-section roentgenography (planigraphy).

Cardiac Catheterization. The hemodynamic pattern in patients with diffuse myocardial lesions has been extensively studied by right heart catheterization (Hetzel et al, Burwell and Robin, Balchum et al). The data obtained were similar to those which have been described as characteristic of constrictive pericarditis There was a reduced, relatively fixed cardiac output and an increased AV oxygen difference The right atrial pressures were markedly elevated, and the pressure pulses showed an "M"-shaped *type of curve*. The systolic pressures in the right ventricle were only moderately elevated, but *the end-diastolic pressures were high*. The right ventricular pressure pulses showed an *early-diastolic* dip and *a late-diastolic plateau* The pulmonary artery pressures and pulmonary wedged pressures were moderately elevated

It is the general consensus of opinion that any diffuse, nonvalvular lesion of the endocardium, the myocardium, or the pericardium which prevents the normal filling of the right ventricle or interferes with systolic ejection of blood will produce a similar hemodynamic pattern. Recently, however, an attempt at hemodynamic differentiation of diffuse myocardial disease from constrictive pericarditis on quantitative grounds has been made (Nye et al) Thus, constrictive pericarditis should be favored when (1) the right ventricular end-diastolic pressure is one-third or more of the systolic pressure, (2) the early-diastolic dip does not reach the base line, (3) the right atrial mean pressure is above 15 mm Hg, (4) there is little or no respiratory variation in mean atrial pressure or in the shape of the atrial pressure contour, (5) there is an abrupt rise and a high plateau after the Y descent, forming an atrial M or W complex. The less well these criteria are fulfilled, the more likely it is for the lesion to be diffuse myocardial disease

The hemodynamic data from the left atrium and ventricle in constrictive pericarditis have been shown to be similar to those obtained from the right heart. The value of left heart catheterization in the presence of primary myocardial disease, therefore, would be (1) to identify *left* heart failure as a factor in the pulmonary *hypertension* of myocardial incompetence by *demonstrating an elevation of left ventricular end-diastolic pressure* and (2) to differentiate organic from functional mitral stenosis by recording simultaneous pressures from the left atrium and left ventricle during the heart cycle. Obviously, only organic mitral stenosis would be characterized by a diastolic pressure gradient across the valve.

Laboratory Aids in the Diagnosis of Viral and Rickettsial Disease. Refinement of old methods and the development of new ones have reduced the isolation and recognition of viruses to an almost commonplace occurrence, but the impression persists among clinicians that identification of a virus is still a major technologic feat As a result, these methods have not been extensively applied in the study of obscure disease. It does not seem unlikely that viruses, in some instances chronically persistent, dormant, or slow of action, will be found associated with diseases not previously regarded to be of viral etiology.

In many virus diseases, for example, the acute exanthemas, the clinical features are so typical that the diagnosis does not require laboratory studies. This has made recognition of a complicating myocarditis easy in this group of infections. The situation is quite different with viruses such as those belonging to the respiratory group. Here an extended period of time may intervene between the virus infection and the appearance of associated disease phenomena. Because of such latent periods, physicians in the past have failed to make the clinical correlation between the initial virus infection and the subsequent postinfectious myocarditis. Thus the cardiac complication has been interpreted as a "second disease."

been pointed out previously by numerous authors but has failed to make the impression upon physicians which its clinical importance warrants. As a result, the cardiac complications of infections have often been interpreted as a "new" disease. In view of the fact that *hypersensitivity* as a cause of myocarditis is being recognized with increased frequency, every case of myocarditis or obscure heart failure should be questioned as to the recent use of such drugs as the sulfonamides, penicillin, and emetine, or antiserums.

Signs. Signs of myocarditis may be entirely absent. The most frequent signs are *tachycardia* disproportionate to the elevation of temperature, the appearance of *cardiac murmurs,* protodiastolic *triple (gallop) rhythm,* diminished intensity of the 1st heart sound, the development of *cardiac enlargement* or *congestive heart failure* during the course of an acute infection, and sensitivity to relatively small amounts of digitalis (Silber and Saphir).

Less common signs observed in association with myocarditis are *hypotension,* a fall in blood pressure without necessarily reaching hypotensive levels, or the presence of a small pulse pressure. Occasionally *circulatory collapse* may occur *Pulsus alternans* has been reported but is an uncommon sign of myocarditis Recurrent pulmonary or systemic *emboli* are not uncommon in cases of myocarditis characterized by intractable heart failure. Rarely, unexpected *sudden death* may be the sole dramatic sign of an unrecognized myocarditis

TACHYCARDIA DISPROPORTIONATE TO FEVER Tachycardia out of proportion to the height of fever is frequently seen in the presence of myocarditis. It is a less reliable sign, however, than is generally considered to be the case, severe toxemia, hypotension, or peripheral circulatory failure may produce such a tachycardia during an acute infection in the absence of injury to the heart It may occur in postinfectious neurocirculatory asthenia This relationship between pulse and temperature is more often seen in rheumatic fever than in myocarditis due to other causes The finding of disproportionate tachycardia should always suggest the possibility of occult myocarditis, but it cannot, in the absence of other evidence, establish the diagnosis.

BRADYCARDIA. This is not infrequent in instances of myocarditis. Sinus bradycardia may occur in rheumatic pancarditis, particularly in young patients. Heightened vagal tone and an adaptive mechanism whereby compensation is maintained by dilatation rather than by tachycardia are theories which have been proposed to account for this finding. A slow pulse in the presence of myocarditis may be indicative of heart block. Such disturbances are commonly encountered in diphtheria, rheumatic fever, and Chagas' disease.

ALTERATION OF THE FIRST HEART SOUND. Another frequent sign of myocarditis is a change in the character of the 1st heart sound This finding is present in approximately half the cases of myocarditis with abnormal ECGs The altered heart tone is characterized by a decrease in intensity and the development of a *muffled* quality. Occasionally an *actual splitting* is apparent. When tachycardia is present, the change in character of the 1st sound may produce a "tic-toc rhythm" or "embryocardia." In most cases, the mechanism responsible for the altered 1st sound is unknown In a number of instances, prolonged AV conduction is the underlying mechanism. The presence of this sign is not evidence of impairment of ventricular contraction A decreased 1st heart sound in the presence of tachycardia should suggest the possibility of myocarditis because, in other conditions associated with rapid heart rate (fever, anemia, hyperthyroidism, etc.), the intensity of the 1st heart sound is usually increased

TRIPLE RHYTHM.[1] In the absence of preexisting heart disease, the appearance of a true protodiastolic type of triple rhythm (gallop rhythm) during the course of an acute infection is reliable evidence of myocarditis. While a serious sign, it does not necessarily signify irreversible myocardial damage. Protodiastolic triple rhythm may be found in acute or chronic myocarditis When it persists after full digitalization, it is an ominous sign.

The pathogenesis of the protodiastolic type of triple rhythm is still controversial. The generally accepted explanation is that it is produced by the entry of blood into a dilated left ventricle during the rapid inflow phase of filling For this reason, the heart will invariably be found to be enlarged

[1] See also Part 3, Chap. 9. *Editor.*

which determine whether the site of predilection of these viruses will be the myocardium or the pericardium Although in most instances the clinical pictures of these two diseases are quite distinct, the diagnosis may be rendered difficult by the occurrence of a myopericarditis In such cases, clinical and electrocardiographic evidence of myocardial injury may persist for months or years.

In *acute benign pericarditis,* chest pain is typically pleuritic in character, but it is subject to such extreme variability in occurrence, distribution, and intensity that differentiation from the precordial oppression of myocarditis may not be possible. A history of concomitant or previous respiratory infections is frequent in both conditions as are fever, malaise, and dyspnea. Examination of the precordium usually clarifies the diagnosis A pericardial friction rub is heard in 70 per cent of the cases of acute pericarditis It may, however, be evanescent and overlooked Gallop rhythm and murmurs which are common in myocarditis are rare in pericarditis, although a "pericardial click" may simulate a gallop In pericarditis, when the heart tones are altered, both sounds are muffled and distant In myocarditis, alteration of the 1st sound at the apex is the rule The circulation time is usually normal in pericardial effusion; it is prolonged when cardiac dilatation is marked or when congestive heart failure is present The apex impulse is palpated well inside the border of cardiac dullness in the presence of pericardial effusion, whereas the apex impulse and border or cardiac dullness coincide when cardiac dilatation is the basis of enlargement

Nonspecific pericarditis may be a chronic disease with a syndrome suggesting congestive failure and may be confused with myocarditis The tendency for the disease to progress to chronic constrictive pericarditis ultimately clarifies the true nature of many such cases

There are several rare disorders which enter into the differential diagnosis of chronic myocarditis Even after exhaustive study, these diseases often cannot be ruled in or ruled out with certainty Amyloidosis, *hemochromatosis,* endocardial fibroelastosis, "idiopathic ventricular hypertrophy," beriberi heart disease, "postpartum" heart disease, and myocarditis due to hypersensitive reactions are examples of such entities

The heart may be involved by either *primary or secondary amyloidosis,* but the former is more common. Although heart failure is the predominant feature, a picture resembling chronic constrictive pericarditis has been described. When coronary artery infiltration is marked, precordial pain or actual myocardial infarction may occur. Liver biopsy is the best means of establishing the diagnosis

Hemochromatosis is an occasional cause of heart failure, but the other manifestations of the disease should simplify the diagnosis. Arrhythmias are common. The incidence of congestive heart failure is higher in young patients with hemochromatosis. Older patients with extreme pigment deposition may show no clinical evidence of myocardial disability.

Endocardial fibroelastosis is still another disease to be distinguished from chronic myocarditis The condition is in most instances found in infants under 1 year of age but has been described in children and adults as well. In the adult, the clinical picture is one of intractable heart failure, complicated by frequent emboli from mural thrombi The antemortem diagnosis is always presumptive and is made by exclusion

Beriberi heart disease is always mentioned in the differential diagnosis of congestive heart failure of undetermined etiology, but is rare in this country. Actually the diagnosis should provide no difficulty if certain criteria are followed such cases, in addition to heart failure, are characterized by a history of a prolonged period of grossly inadequate nutrition, evidence of peripheral neuropathy. *For pellagra,* the absence of other causes of heart disease and improvement after specific therapy are basic data for diagnosis

Hypertrophy of the heart and congestive heart failure without a recognizable etiology have been reported in approximately 60 cases and termed "idiopathic ventricular hypertrophy." The disorder enters into the diagnosis of chronic myocarditis because in both conditions the clinical picture is essentially identical The predominant histologic findings in the myocardium are hypertrophied muscle fibers, degenerative changes, connective tissue proliferation, and minimal degrees of cellular infiltration. *Myocardial fibrosis* is an end stage which is reached regardless of the nature of the initial injury. The histologic find-

through the medium of left heart catheterization.

SENSITIVITY TO DIGITALIS. A valuable clue suggesting the possibility of myocarditis in patients with congestive heart failure is the occurrence of disturbances of rhythm with relatively small doses of digitalis (Silber et al.). In one report this phenomenon was observed in 36 per cent of the cases of myocarditis (Silber). The manifestations of sensitivity consisted of the development of first- or second-degree AV block or the occurrence of bigeminy due to ventricular premature systoles. Contrary to prevalent medical opinion, digitalis was generally as effective in its cardiotonic effect in the heart failure associated with myocarditis as that due to other etiologies.

LABORATORY AIDS IN THE DIAGNOSIS OF MYOCARDITIS

The Electrocardiogram. The ECG is the most important laboratory aid in the diagnosis of myocarditis. *Abnormalities of the ECG consistent with myocarditis occur in approximately one-third of patients during the course of acute infectious diseases* (Fine et al.). In those instances where clinical manifestations are absent, the diagnosis may rest entirely on the findings of serial ECGs. Despite its importance, the use of the ECG in the diagnosis of myocarditis is fraught with limitations. Occasionally, the ECG is normal shortly before necropsy reveals diffuse myocardial damage. On the other hand, one may be misled by abnormalities of the ECG produced by extracardiac factors during the course of acute febrile diseases. Some of them are shifts in pH, alteration of serum electrolytes, hyperpyrexia, hypotension, or the effect of drugs which influence the contour of the ECG.

The S-T segment and the T wave are the portions of the ventricular complex which are most strikingly altered in the presence of myocarditis. The most common changes consist of *diminution or inversion of the T wave* both in the limb leads and in a variable number of precordial leads. At times, these inverted T waves may resemble "coronary" T waves. In chronic myocarditis, the T-wave changes may persist, and in some cases, the ECG may assume the pattern of "left heart strain." *A left heart strain pattern* may also be the residue of a healed myocarditis in which the heart is normal to all other methods of examination (Silber et al.). Displacement of the S-T segment is seldom striking and is usually an early and evanescent sign. As a rule, by the time the T-wave inversion has appeared, the S-T segment has returned to the isoelectric line and is normal.

Disturbances of rhythm are common in the presence of myocarditis. *Sinus tachycardia* is most frequent; sinus bradycardia is occasional. *Atrial, nodal,* or *ventricular premature systoles* are frequent. *Atrial fibrillation* is encountered in an occasional case of diphthentic or "Fiedler's" myocarditis; *atrial flutter,* less often. *Ventricular tachycardia* occurs principally in terminal cases of diphthentic myocarditis.

Atrioventricular or *intraventricular conduction disturbances* are most frequent in diphthentic myocardities and in Chagas' disease, but may be encountered with any diffuse, extensive inflammation of bacterial, viral, or rickettsial origin. *Right bundle branch block* occurs almost without exception when intraventricular conduction is impaired in Chagas' disease.

Low voltage may be seen either in the presence of marked cardiac dilatation or when there is an associated pericarditis with effusion. Since the electrocardiographic findings of pericarditis are due to the underlying subepicardial myocarditis, differentation of myocarditis from pericarditis cannot be made solely on the basis of electrocardiographic criteria.

Studies of the Q-T interval have been largely limited to rheumatic myocarditis, but *Q-T prolongation* has been reported in the myocarditis of measles, influenza, viral hepatitis, and poliomyelitis (Lyon).

Radiographic Findings. The radiographic findings are not distinctive in acute or chronic myocarditis. When the heart is not dilated, its radiographic silhouette will be normal. When clinical disability is significant, with or without congestive failure, *dilatation* will be present. Under these circumstances, radiographic enlargement will be demonstrable. In chronic myocarditis with intractable failure, dilatation may be extreme, and cardiac pulsations as seen fluoroscopically may be markedly decreased or absent. With such a heart, differentiation from a large pericardial effusion may

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in the T waves and S-T-segment depression. Since a "cure" of bacterial endocarditis has become frequent with the use of antibiotics, the prognosis of this disease has come to depend upon the severity of the complicating myocarditis rather than the residual valve damage. Unfortunately, the myocarditis does not respond so well to the antibiotics as do the endocardial lesions.

In the so-called *isolated myocarditis*, the prognosis is inevitably poor. Therapy does not alter the prognosis even in those instances where the correct diagnosis is made early in the disease. Hope for these patients is to be found in the reports of an occasional case that appears to be benefited by the administration of corticotropin or the adrenal steroids.

TREATMENT

The treatment of myocarditis involves both prophylactic and supportive considerations. Myocarditis can be averted by preventive measures or adequate treatment of the causative infectious disease. Thus diphtheria can be prevented by immunization, and the occurrence of diphtheritic myocarditis can be reduced by the prompt administration of adequate amounts of antitoxin and penicillin. Prophylactic chemotherapy before and after operative procedures in patients with rheumatic and congenital heart disease can prevent bacterial endocarditis. Likewise, intensive treatment of bacterial infections, especially those due to streptococci, will reduce the incidence of such myocarditides. Several of the rickettsial diseases and the viruses of the psittacosis-lymphogranuloma group respond to the broad-spectrum antibiotics.

The most important supportive measure in the treatment of myocarditis is *bed rest* until all manifestations of an active myocardial process have disappeared. During this time, the excessive administration of parenteral fluids should be avoided. Arrhythmias that do not threaten life should not be overtreated since they usually spontaneously disappear as the inflammatory process subsides. If atrial flutter or fibrillation produces a rapid ventricular rate, sufficient digitalis should be given to achieve a normal rate. For this purpose, the rapidly excreted glycosides are the digitalis preparations of choice so that, if toxic manifestations occur, they will not be protracted. Potassium orally or intravenously is effective in terminating digitalis-induced arrhythmias.

When heart failure appears during the course of myocarditis, it is managed in the same way as in other types of heart disease. When digitalis, salt restriction, and diuretics have failed to restore compensation, corticosteroids may effect recovery or temporary improvement. The use of *long-term anticoagulant therapy* is indicated for those cases of acute or chronic myocarditis characterized by intractable failure because of the occurrence of frequent thromboembolisms in this group of patients.

Electrocardiographic abnormalities may persist after clinical recovery has occurred in the patient with myocarditis. Bed rest should be enforced only if the ECG is unstable, showing evidence of either continuing progression or regression. Once the ECG has become stabilized, regardless of whether this is characterized by a normal or abnormal pattern, the rate of ambulation of the patient is governed by the clinical status in conjunction with adjuvant laboratory tests of "activity."

In our present state of knowledge, the treatment of choice of myocarditis due to hypersensitive reactions appears to be the use of *corticosteroids*. These hormones should be administered in adequate doses without regard for the metabolic complications of these agents, which are seen only after prolonged administration. Fluid retention, should it occur, is readily controlled by the use of mercurial diuretics or potent oral diuretics such as *chlorothiazide*. The patient should be impressed with the necessity of avoiding in the future the administration of the drug which has precipitated the myocarditis.

SPECIFIC TYPES OF MYOCARDITIS

Myocarditis may be classified in a number of ways. An *etiologic classification*, while unsatisfactory to the pathologist, is useful from the clinician's point of view. Accordingly, the specific kinds of myocarditis to be discussed in this section are classified etiologically as follows.

INFECTIOUS MYOCARDITIS

Myocarditis associated with bacterial infections.
- Tuberculosis
- Diphtheria
- Scarlet fever

Three general types of laboratory examination are used to diagnose viral and rickettsial disease. They are (1) serologic tests, (2) isolation of the virus, and (3) histologic examination.

Serologic tests constitute the most practical technique. These methods comprise complement-fixation, neutralization, and hemagglutination tests. *Complement-fixation* is the serologic test of choice for the routine diagnosis of many viral and rickettsial diseases. A fourfold or greater rise in the antibody titer of convalescent serum as compared to that of serum obtained during the acute phase of the illness is of diagnostic significance. The *heterophile agglutination test* for infectious mononucleosis and the *cold hemagglutination test* for certain of the viral pneumonias are nonspecific tests which are also of considerable diagnostic aid. *Neutralization tests* are too difficult and too hazardous for the average hospital laboratory.

The development of simplified *tissue-culture techniques* has increased the possibilities of a wider range of virus diagnostic tests. Animal and chick-embryo inoculation, while informative, are not for the hospital laboratory, since they are expensive, time-consuming, and potentially dangerous.

Microscopic examination is of limited usefulness because few viruses produce inclusion bodies that are diagnostic. Moreover, many viruses produce similar pathologic lesions. Finally, appropriate tissues for antimortem study are seldom available.

DIAGNOSIS

When myocarditis occurs during the course of an acute infection, there is difficulty in differentiating the signs and symptoms of the primary disease from those due to the heart involvement. Weakness out of proportion to the severity of the primary disease, palpitation, precordial oppression or pain, or dyspnea should suggest myocarditis. Such symptoms, together with one or more of the signs of myocarditis and a compatible electrocardiographic picture, are adequate evidence for the diagnosis of myocarditis. Congestive heart failure occurring during the course of an acute infection in a patient without previous heart disease is virtually pathognomonic of acute myocarditis. Patients are seen who manifest no symptoms despite the presence of signs of myocarditis, such as triple rhythm, tachycardia, murmurs, etc. In other patients, the ECG may be the sole evidence of acute cardiac damage.

Signs and symptoms of myocarditis, occurring after a latent period following an infection, readily suggest the diagnosis because confusion with the primary disease is not a factor. Marked asthenia, dyspnea, or precordial oppression are suspicious of postinfectious myocarditis. Neurocirculatory asthenia following an infection may mimic myocarditis, but the absence of electrocardiographic abnormalities and signs of heart disease and familiarity with the patient's personality permit ready differentiation of the two conditions. Occasionally, what is initially thought to be myocarditis following influenza actually proves to be myocardial infarction.

Chronic myocarditis usually is manifested by unexplained cardiomegaly or by the signs and symptoms of intractable heart failure. Triple (gallop) rhythm, hypotension, small pulse pressure, atrial fibrillation, and the *frequent occurrence of pulmonary emboli* are the most characteristic features. Systemic emboli are occasionally observed. Death may occur abruptly after an illness of a few weeks or after one or more years of unremitting cardiac disability. Some patients may have exacerbations and remissions and ultimately make a complete recovery. Myocarditis as the cause of protracted heart failure may go unrecognized if a preceding acute infection, usually of the respiratory tract, remains undisclosed. The opinion has been expressed that most of such cases are due to "grippe" (Wuhrmann).

Chronic myocarditis may be mistaken for *rheumatic mitral valve disease* when similar murmurs are present at the apex. The abrupt onset of congestive heart failure in adults without rheumatic history should suggest postinfectious or hyperergic myocarditis. A middiastolic murmur alone is not necessarily pathognomonic of mitral stenosis. The confirmatory signs should be sought, namely, an opening snap, accentuated apical 1st sound, and evidence of right heart strain in the ECG. The latter is seldom seen as a result of diffuse myocardial disease. Cases may masquerade for long periods of time as mitral stenosis until demonstrated to be instances of chronic malignant myocarditis at autopsy (Silber and Shaffer).

At times, there may be difficulty in differentiating *acute benign pericarditis* from acute myocarditis. Both diseases have been reported due to Coxsackie B or influenze A or B infection. Nothing is known of the factors

tionship was found between the severity and extent of the pneumonia and the degree of myocardial changes. Myocardial involvement apparently occurs relatively early in the course of the disease or when there is a recent spread of the disease. Myocardial lesions may accompany a pneumococcic endocarditis or pericarditis, or nonspecific myocardial lesions may occur without local bacterial involvement of the heart.

In the absence of preexisting heart disease, there is no good evidence to indicate that the myocardial lesions are responsible for serious dysfunction of the heart. Transient electrocardiographic changes consisting mainly of *low or inverted T waves* have been observed in approximately 25 to 45 per cent of cases.

PYEMIA. Acute myocarditis and multiple abscesses may be a metastatic manifestation of an overwhelming staphylococcal or streptococcal sepsis. It is doubtful that these lesions are of clinical significance in these fatal cases. Rarely such an abscess may be the cause of cardiac rupture.

MENINGOCOCCEMIA AND GONOCOCCEMIA. Meningococcal or gonococcal myocarditis in the absence of concomitant endocarditis is so rare that it is not possible to describe any representative clinical picture. At times, myocarditis may be associated with meningococcal meningitis and produce the clinical picture of heart failure.

Brucellosis. The heart is infrequently involved in brucellosis, and then endocarditis is the most frequent lesion. Rarely, an interstitial myocarditis has been described (Amuchastegui and Herrero). Nonspecific electrocardiographic changes have been described, and definite clinical evidence of myocardial involvement has been reported (Panuccio). Of considerable interest is a report suggesting that calcific aortic stenosis may be due to healed brucellosis (Peery).

Salmonellosis. Myocarditis in these infections is rare. Mild degenerative changes, such as may be seen in many infections, are more often reported. As in diphtheria, *peripheral circulatory collapse* occurs rather than primary cardiogenic shock. Congestive heart failure is extremely rare. Electrocardiographic changes consisting primarily of *flat or inverted T waves* have been observed in the majority of cases of typhoid fever either during the acute illness or during recovery.

Bacterial Endocarditis. In addition to acute myocarditis, the myocardium in bacterial endocarditis may be the site of hemorrhages, foci of necrosis and abscesses, minute infarcts, emboli, perivascular infiltrations or fibrosis, and Aschoff bodies. Diffuse myocarditis has been reported in 24 to 43 per cent of cases of bacterial endocarditis. The alarming frequency of cardiac failure in "cured" cases of bacterial endocarditis has led to the realization that the myocardial lesions play a greater part in determining the subsequent cardiac status than does residual valve damage.[2]

MYOCARDITIS ASSOCIATED WITH RICKETTSIAL INFECTIONS

Tsutsugamushi disease, Rocky Mountain spotted fever, and *epidemic typhus,* in this order, are the human rickettsial diseases of importance from the standpoint of cardiac involvement. Cardiovascular lesions are inconspicuous in *Q fever, trench fever,* and *rickettsialpox.* The pathologic changes in the myocardium consist of either focal lesions or a more diffuse interstitial myocarditis.

The clinical importance of the myocarditis in these diseases is problematic. Good correlation between symptoms and demonstrable myocardial lesions has not been shown. *Circulatory collapse,* the outstanding feature of rickettsial disease, is the result of changes in the peripheral circulation. Congestive heart failure is seldom found either in the acute stages of these diseases or during convalescence in the absence of preexisting heart disease. Signs of cardiac involvement are usually not present until the second week of illness and are then most frequently limited to *diminished intensity of the 1st heart sound, systolic murmurs,* and minor degrees of cardiomegaly.

Abnormal electrocardiographic patterns occur but are not distinctive. Flattening or inversion of T waves, S-T depression, varying degrees of AV block, BBB, and transient arrhythmias of all types have been described. These abnormalities are usually transient, and evidence in the ECG of permanent myocardial damage is rare.

[2] See also Chap. 1. *Editor.*

ings, therefore, do not indicate whether an inflammatory, toxic, or degenerative process is responsible for the disease. It is likely that idiopathic cardiac hypertrophy will ultimately prove to be a "burned-out" stage of a myocarditis due to an infectious agent or to hypersensitivity.

The effects of *hypersensitive reactions* on the heart have only recently become the object of attention. Numerous instances of such cardiac involvement have recently been reported from the use of emetine, penicillin, antiserums, and sulfonamides. The validity of the clinical diagnosis of myocarditis due to drug sensitivity is supported by extensive experimental and pathologic studies. Myocarditis associated with hypersensitive reactions is often mistaken for infectious myocarditis because the responsible drug is administered during the course of an infection or because the symptoms of fever and myocarditis due to the drug suggest an infectious disease.

In mild reactions, no cardiac manifestations are apparent In more severe cases, triple rhythm, cardiomegaly, systolic murmur, and pericardial friction rubs and effusion may occur Electrocardiographic abnormalities may be minor or conspicuous, then, T-wave inversion and S-T deviation may be striking. In the acute stage, prominent Q waves in the limb leads, QS complexes in the chest leads, or coronary-like T waves may be seen. Extrasystoles, paroxysmal tachycardia, atrial fibrillation, and BBB have all been reported. It my ultimately be established that many cases of "isolated myocarditis" or "idiopathic ventricular hypertrophy" are due to severe, irreversible heart damage in response to drug sensitivity.

There are a number of references in the medical literature of the past 20 years describing heart failure which appeared in the last month of pregnancy or the first few weeks of the puerperium in the absence of any recognizable preexisting cardiac lesion (Meadows) Heart failure in this group of patients has been designated as "postpartum heart disease" or "postpartum myocarditis" In none of the reported cases has any evidence been presented that such heart disease is causally related to pregnancy, aside from their coincident occurrence. Recently, reports have appeared which point to virus infections and sulfonamide sensitivity as the etiologic basis for several such cases. Such evidence serves to point out that diffuse myocardial disease in the puerperium may be related to a variety of etiologic agents. Until more knowledge is available it seems warranted to consider cases of "postpartum" heart disease as instances of postinfectious myocarditis or hypersensitive myocarditis and not as a separate entity.

PROGNOSIS

It is difficult to make an accurate statement about the prognosis of myocarditis because so few cases of the nonrheumatic types are diagnosed clinically. It is necessary to consider the prognosis in terms of the disease of which it is a complication or a manifestation. Fine and associates maintain that most patients who have myocarditis during an infectious disease survive without any significant residual effects. Such a conclusion, however, does not take into account that few cases are recognized at the bedside and that the relationships of postinfectious myocarditis to antecedent infection is so often overlooked. The outlook for patients with myocarditis of undetermined etiology is usually grave.

In *diphtheritic myocarditis*, the prognosis is excellent if there is no evidence of cardiac involvement during the first 10 days. In these cases a 2 per cent mortality has been found in contrast to 11 per cent in those patients with evidence of myocarditis prior to the tenth day. It is rather extraordinary that, despite the frequent clinical severity of diphtheritic myocarditis and the widespread pathologic damage reported, significant residual myocardial damage is seldom demonstrable. Recently, evidence of permanent cardiac damage as a result of diphtheria has been reported. In two patients, the heart disease followed a subacute course, with varying symptoms for several years (Hoel and Berg). Another patient showed persistent abnormalities of the ECG for 12 years, ultimately dying of congestive heart failure Diffuse fibrosis throughout the myocardium with normal coronary vessels was revealed at autopsy (Sayers) The remaining cases of permanent cardiac damage exhibited various electrocardiographic abnormalities consisting of prolonged AV conduction, BBB, complete heart block, and nonspecific changes

the influenza and the resultant cardiac damage Cardiac complications are infrequent during the acute stage of the disease. The vast majority of such complications occur during convalescence and often long after apparently complete recovery from the primary infection. This is apparently as true for children as for adults (Muller). Influenza myocarditis was described as appearing in these children 10 to 30 days after an attack of influenza.

There are virtually no published reports regarding cardiac involvement by the Asian strain of influenza during the pandemic of 1957. In the report of the Bombay Influenza Research Committee, the incidence of clinically evident myocarditis was 3.3 per cent in the mild cases and 5.7 per cent in the severe cases Abnormal ECGs were seen in 20 per cent of cases. The findings were consistent with myocarditis in 13 per cent and showed nonspecific changes in 6 5 per cent There were two cases of first-degree AV block (1.6 per cent) but no disorders of rhythm Protracted severe myocarditis terminating in death has been observed as a result of Asiatic influenza (Silber) From such scant preliminary information, it does not appear that Asiatic influenza differs notably in its effect upon the heart from other strains of influenza virus

Primary Atypical Pneumonia. The clinical syndrome of "primary atypical pneumonia" may be produced by a number of different etiologic agents, bacterial and fungal as well as viral Primary atypical pneumonia (PAP) virus producing cold hemagglutinins has been isolated from patients Cold agglutinins, however, have been of value in establishing the diagnosis in only a portion of such cases The adenoviruses induce respiratory disease consistent with the syndrome of primary atypical pneumonia without producing cold hemagglutinins In view of the varied etiology of this syndrome, it is not possible to describe comprehensively the cardiac complications of the primary atypical pneumonias

Electrocardiographic evidence of myocarditis has been reported in about 4 per cent of cases These changes consisted of S-T-segment displacement, low or inverted T waves, and aberrations of AV or intraventricular conduction Abnormal ECGs occurred with or without clinical evidence of cardiac embarrassment Electrocardiographic patterns of acute pericarditis have been described. This is not unexpected in view of the numerous reports of "benign idiopathic" pericarditis following in the wake of atypical pneumonia Fulminating, rapidly fatal myocarditis as well as acute and subacute forms with complete recovery have been attributed to the viruses producing the clinical picture of "atypical" pneumonia (Silber et al).

Coxsackie B. The Coxsackie B group of viruses are associated with a wide variety of clinical disorders. Myocarditis has been produced in mice inoculated with certain group B strains. It is now established that similar cardiac lesions have occurred in man as a result of infection with group B type 3 Coxsackie virus. Not only has histologic evidence of myocarditis been demonstrated in fatal human cases, but the virus has been recovered from the spinal cord in one such instance. In these patients (all of whom were infants), extreme tachycardia was the only clinical manifestation of myocarditis A clinical picture of "acute benign" pericarditis has been described as a consequence of infection with type 4 and type 5 Coxsackie group B viruses T-wave inversions in the limb and precordial leads characteristic of myopericarditis were present in these cases. In one instance, AV nodal rhythm was present.

Poliomyelitis. Morphologic changes indicative of myocarditis have been described in 30 to 100 per cent of cases in which autopsies were performed. The lesions vary from focal collections of lymphocytes in the interstices to actual muscle necrosis with extensive neutrophilic infiltration. It has been suggested that most of the changes are due to hypoxia, but recent data support the concept that myocarditis is produced by direct viral invasion of the heart. Isolation of the virus of poliomyelitis from the hearts of two fatal cases, as well as from the hearts of experimental animals, have been achieved

The clinical recognition of myocarditis in the presence of poliomyelitis is difficult. Except for cardiomegaly or congestive heart failure, the signs and symptoms are relatively nonspecific Dyspnea, cyanosis, tachycardia, and hypotension may be the result of spinal cord or medullary involvement, as well as airway obstruction, and are of little value in the differential

- Septicemia:
  - Pneumococcus
  - Staphylococcus
  - Streptococcus
  - Other acute bacteremias
- Brucellosis
- Salmonellosis
- Bacterial endocarditis

Myocarditis associated with rickettsial infections:
- Tsutsugamushi disease (scrub typhus)
- Rocky Mountain spotted fever
- Epidemic typhus

Myocarditis associated with viral infections:
- Influenza
- Coxsackie virus
- Poliomyelitis
- Primary atypical pneumonia
- Infectious mononucleosis
- Psittacosis
- Measles
- Encephalomyocarditis virus, etc.

MYOCARDITIS ASSOCIATED WITH BACTERIAL INFECTIONS

The high degree of effectiveness of modern antibiotic therapy against bacteria and the success of prophylactic immunization have resulted in a marked reduction in the incidence of bacterial myocarditis It now occupies a position distinctly secondary in importance to the viral myocarditides There remain, nevertheless, a number of important gaps in our knowledge with respect to bacterial myocarditis. For example, while the histopathology of the acute stage is well delineated, much less is known about the intermediate and end stages of these diseases In relatively few of the myocarditides due to bacteria and fungi are organisms actually found within the myocardium itself, and in most of these diseases, it is still unsettled whether the myocarditis is due to *direct damage*, to a *toxic effect*, or to *hypersensitivity* to some portion or some elaboration of the microorganism.

Tuberculosis. Tuberculosis of the myocardium is rare Miliary, nodular, and diffusely infiltrating lesions have been described The nodular type is most frequent. The myocardium is most often involved by extension of lesions from a contiguous *tuberculous pericarditis*. The greater percentage of miliary lesions are found in children.

Myocardial tuberculosis is usually asymptomatic. Involvement of the atria by nodular or infiltrating lesions may occasionally produce any of the atrial arrhythmias.

Diphtheria. By careful clinical study, myocarditis is recognizable in early 50 per cent of patients with diphtheria. The ECG provides the earliest evidence of cardiac involvement. Myocarditis may occur during the first few days of the illness, or it may not be present until the third or fourth week. Myocarditis clinically apparent during the first 10 days is usually severe, while that appearing after 10 days usually carries an excellent prognosis. Evidence of moderate degrees of congestive failure is common but is usually dominated by the concomitant picture of *peripheral vascular collapse*.

The *ECG* is abnormal in about 50 per cent of patients with diphtheria if frequent records are taken. The commonest findings are abnormalities of S-T and T. A number of arrhythmias may occur, including premature beats, dropped beats, atrial flutter or fibrillation. *Bundle branch block* and *AV block* are frequent, but the latter is not the most common abnormality as has been stated in the past.

It is becoming increasingly evident that diphtheritic myocarditis may produce permanent anatomic and functional damage.

Scarlet Fever. Myocarditis associated with scarlet fever is not rare from a pathologic point of view. Myocardial lesions are found in 70 per cent of fatal cases and consist primarily of inflammatory involvement of the interstitial tissue This type of lesion has also been described in the hearts of patients who have died of streptococcal bacteremia. It is impossible, on the basis of clinical grounds alone, to distinguish the myocarditis which occurs after scarlet fever from that of rheumatic fever.

Approximately 5 to 15 per cent of patients with scarlet fever or streptococcal pharyngitis have *abnormal ECGs*. The most frequent abnormality has been *prolongation of the P-R and Q-T intervals*, but minor S-T depressions and lowering or inversion of the T waves are not uncommon.

Septicemia. PNEUMONIA. Pathologic reports of the myocardial lesions in pneumococcal pneumonia vary from insignificant degenerative changes to significant myiocarditis in as high as 38 8 per cent of patients. No rela-

10

Echinococcus disease of the heart

EDUARDO J. CANABAL AND JORGE DIGHIERO

ETIOLOGY

Human echinococcosis (hydatid disease) is caused by the development of the larval stage of *Taenia echinococcus*, a cestode tapeworm whose definitive host in most instances is the dog

Taenia echinococcus is small in size (5 to 8 mm), having a *head*, a *neck*, and *three body segments* (Dévé, Dew) Ordinarily, many thousands live fixed to the mucosa of the small intestine of the host The head (½ mm long) is composed of a muscular protractile rostrum, showing two lines of booklets and four suckers by which the parasite anchors itself to the mucosa A neck unites the head to three body segments The last ring (proglottid) containing the sexual organs, when mature, shows a gravid uterus with an average of 800 to 2,000 ova (oncospheres), which are composed of an external vitelline membrane encircling the hexacanth *embryo* The *oncospheres*, when shed with the feces of the dog, contaminate grass and water and are ingested by the intermediate host (usually sheep) Because of his close association with infested dogs in rural areas, man is also prone to contamination

In the presence of *intestinal juices*, the oncosphere germinates, giving rise to a vesicle or *hydatid* which attains its maximum size in 72 hr, fading thereafter The vesicle penetrates into the *intestinal* capillaries by ameboidism, progressing later along the blood stream (portal *circulation*, first) When its size is bigger than that of the capillary lodging it, it *becomes fixed*

The liver is, by *far*, the most commonly attacked organ (first capillary barrier), but the liver is frequently spared because of the rather small size of the hexacanth embryo and the distensibility of the hepatic capillaries. Thus, the embryo can reach the pulmonary capillary circulation, where it may become lodged (pulmonary hydatid cysts are second to hepatic cysts in frequency). This barrier *can also be overcome* by the embryo, which may then progress to the systemic circulation via the left heart chambers.

Once at its final destination, the embryonal vesicle keeps growing, thus starting the larval phase *of the parasite The hydatid* vesicle (water vesicle) is composed of an outer elastic membrane of chitinous nature (cuticle) lined by an inner germinative layer (fertile membrane) containing a colorless and highly allergenic fluid called *hydatid fluid*.

The germinative layer of the primitive hydatid vesicle (mother vesicle) gives rise, by a process of proliferation, to the proligerous capsules (brood capsules) which may float *in the fluid, another* product of the germinative layer. From these capsules, the *scolex* (larval asexual phase of *Taenia echinococcus*) generates. Like the head of the adult form of the taenia, it shows a rostrum, four suckers, and a double line of booklets (38 in number) (Perez-Fontana).

During the *first period* of evolution in the intermediate host, the hydatid vesicle remains sterile (no proligerous capsules and, of course, no germinative elements, scolex). With the passing of time and when living conditions are *disturbed* by nutritive or mechanical *factors, the* hydatid vesicle becomes fertile Ultracentrifugation of the hydatid *fluid at this* time reveals the presence of hydatid "sand," composed of innumerable brood *capsules* and scolices.

The process of growth of the hydatid vesicle is constantly menaced by *several factors* (mechanical, toxic, *infectious, allergic*). Various changes in the *mother* vesicle may result. Besides those taking place in the hydatid membrane (*senescence*, rupture, etc.), the germinative *elements* (scolices) floating in the hydatid *fluid* undergo vesicular transformation (*daughter* cysts), this represents a

MYOCARDITIS ASSOCIATED WITH VIRAL INFECTIONS

Opinion as to the nature and extent of cardiac involvement by viruses has been greatly revised by investigations of the past 20 years. This has been achieved through detailed histologic examination of the heart in fatal virus infections, by systematic electrocardiographic studies during the course of these diseases, and by experimental work with various viruses. That extended intervals may supervene between the time of a virus infection and the appearance of clinical manifestations has been an important concept in appreciating the role that viruses may play in cardiovascular disease.

Although enormous strides are being made in virology, there is still a paucity of data regarding virus myocarditis in man. Evidence has not been obtained that multiplication of virus occurs within any of the cells of the heart. Even the presence of the agent in the myocardium has been demonstrated only twice, one instance involving the virus of poliomyelitis, the other, a virus of Coxsackie group B. On these two occasions, more cogent information might have been obtained if isolation of the virus had also been attempted from the blood stream. Then, if the virus had been found in heart muscle alone, a concomitant infection with viremia could have been excluded.

The mechanism of cardiac damage by viruses remains under assessment Whether this is due to a direct toxic effect of the virus, or to products of damaged cells, or by indirect effect through growth of the virus elsewhere in the body is not known.

The relationship of virus infection to such obscure conditions as *isolated myocarditis* is undetermined although there is considerable inferential evidence to suggest that this is the case.

Finally, there remains the problem of whether heart damage by viruses may be irreparable and give rise to chronic cardiac disability. Until recently it has been medical doctrine that, if death does not occur during the acute phase of viral myocarditis, recovery is complete. There is a growing body of evidence to indicate that this may *not* be the case There is neither a logical or a scientific reason why rheumatic myocarditis should enjoy a monopoly in the matter of chronicity.

At present there is no specific therapeutic agent known to hold definite promise of success in virus chemotherapy. The outlook, however, is not necessarily hopeless Thousands of compounds are undergoing tests in many research centers, and an effective remedy could be discovered at any time. Meanwhile, the progress which is being made in identifying new viruses, and the diseases for which they are responsible, should provide greater impetus to the search for specific therapy.

Influenza. Heart involvement in influenza has been recognized for a long time, but controversy still exists among both pathologists and clinicians as to the extent and importance of such lesions. The studies of the majority of pathologists have disclosed no characteristic morphologic changes in the myocardium in influenza, and those which did occur were slight. On the other hand, others have expressed the opinion that no other infectious disease produced such widespread myocardial damage (Schmorl, Roulet). Despite the numerous clinical descriptions of cases of epidemic influenza in which evidence of myocardial damage was recognized by symptoms or by electrocardiographic changes, reluctance still exists in acknowledging the connection between influenza and heart disease. This skepticism is due to the difficulty of differentiating influenza from the many other respiratory diseases on the basis of symptomatology alone.

A variety of cardiac symptoms have been described, such as *weakness, dyspnea,* and *precordial pain,* as well as *sudden death. Electrocardiograms* have demonstrated all types of alterations of contour and rhythm. In only two cases of influenza myocarditis was the virus isolated and identified (Finland et al). A single case of acute myocarditis has been reported in which influenza A was identified as the etiologic agent by hemagglutination tests (Borden). A number of cases of myocarditis due to influenza A or B have been reported in which the virus etiology was established by complement-fixation tests. In this report, there was evidence that influenza viruses may be a cause of chronic myocarditis and permanent heart damage (Silber et al.). There is a lack of correlation between the clinical severity of

factors are responsible for a reactive daughter cyst formation (*multivesicular cyst*) and for various changes occurring in the hydatid vesicle (degeneration, senescence, etc.). When one or several of these changes take place, the cystic adventitia becomes inspissated, denser, and partially or totally calcified, causing comparatively more harm to the neighboring cardiac structures In some cases of profound alteration of the primitive hydatid cyst, and amorphous substance (*hydatid putty*) is likely to appear Other histologic changes due to the presence of the parasite in the myocardium (perihydatid granulomas, hydatid pseudotuberculosis, etc) have been described.

During the period of intramural development of the cyst, its presence may be overlooked (especially when growing toward the endocardium), but when it has reached a certain size and points to the pericardial sac, it produces a localized bulge in the cardiac silhouette, a feature which facilitates roentgenologic recognition of the disease A peripheral rim of calcification or spotty areas of calcific density within the abnormal myocardial bulge are of diagnostic significance The pericardium often reacts to the presence of a myocardial cyst by developing adhesions The endocardium, on the contrary, does not react, being therefore easily invaded by the cyst (one or several episodes of rupture)

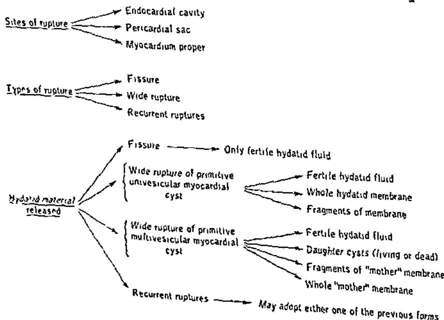
The natural history of the primitive hydatid myocardial cyst is often interrupted by *its rupture* on account of the special conditions of its host and the multiple changes it may undergo during its process of growth, but the cyst can remain living and quiescent for a *long time or* death of the parasite may occur, with subsequent and spontaneous cure of the disease.

Rupture of the cyst can produce a series of complications, depending on (1) the site of rupture (*into the endocardial cavity, the pericardial sac, or the myocardium itself*), (2) the type of rupture (small fissure in the hydatid membrane and the adventitious cyst, wide open rupture, recurrent ruptures), (3) the contents of the primitive cyst (*univesicular* cyst, multivesicular cyst, cyst with different degrees of changes, etc) (Diagram 8-1).

Dévé pointed out that primitive cysts located in the wall of either of the right heart chambers have a natural tendency to rupture into the endocardial cavity, while those in the left ventricle do it more frequently into the pericardial sac.

A small rupture (*fissure*) of a fertile hydatid cyst releases only hydatid fluid containing free scolices and brood capsules. This accident gives rise to (1) a rapid onset of *hyperergic phenomena* of varying intensity, (2) the "sowing" of echinococcal germs (scolices) re-

DIAGRAM 8-1 PROCESS OF RUPTURE OF THE PRIMITIVE MYOCARDIAL HYDATID CYST



diagnosis. The frequency of myocarditis appears to be directly proportional to the severity of the disease.

There is a wide variation in the reported occurrence of *electrocardiographic abnormalities* in acute poliomyelitis, but 25 per cent is a fair approximation of the incidence. A variety of abnormalities have been described. Alterations of S-T, T-wave inversions, arrhythmias such as *premature systoles* and *atrial fibrillation*, prolongations of P-R, and of the QRS and Q-T intervals have all been described. No specific electrocardiographic changes are associated with poliomyelitis; they are those which occur in a variety of infections. Electrocardiographic abnormalities usually appear during the first two weeks of poliomyelitis. Because there are several factors which may be responsible for electrocardiographic changes in poliomyelitis, e.g., hypoxia, hypotension, fever, it has been suggested that only those serial changes which persist for more than 2 to 3 weeks be attributed to viral invasions of the heart and resulting myocarditis (Weinstein).

Measles. Although anatomic involvement of the heart does occur in measles, it is rarely sufficient to be of clinical significance. Clinical manifestations are almost exclusively limited to electrocardiographic abnormalities. The latter consist of changes in the T waves or the P-R interval.

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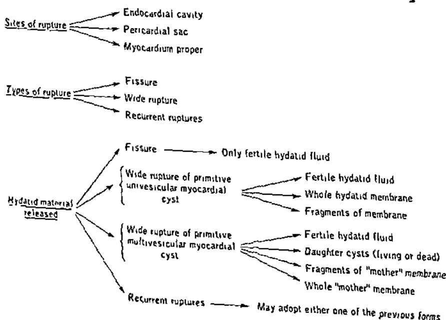
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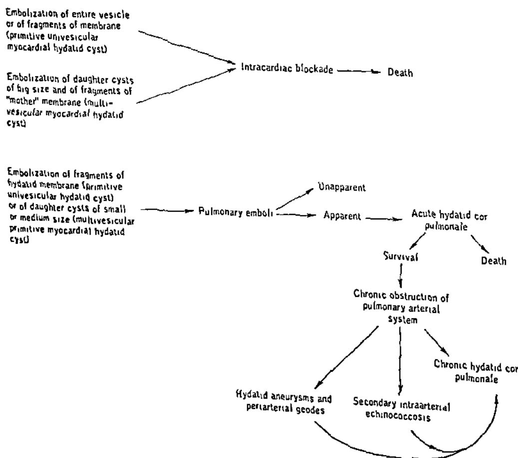
sponsible for the development of secondary echinococcosis. "Every case of secondary echinococcosis presupposes the presence of one or several new cysts derived from *the original cyst.* It implies the effraction of the mother vesicle allowing the liberation, the dissemination, and the colonization (local, surrounding or distant) of living parasitic elements proceeding from the primitive lesion" (Dévé)

The fertile hydatid fluid (highly allergenic) shed into the endocardial cavity (Diagram 8-2), besides producing hyperergic phenomena that can either be fatal, permit the patient to survive, or even be unapparent (depending upon the patient's previous sensitization to the disease), is responsible for late *complications.* These are due to the vesicular transformation of scolices carried by the blood stream to points distant from the site of rupture of the primitive cyst (metastatic echinococcosis of either the lesser or the systemic circulation) Similar complications are seen in cases of hydatid cysts of the liver rupturing into the inferior vena cava.

The arrival of fertile hydatid fluid in the pericardial serous membrane (Diagram 8-5) produces, as an immediate complication, an *acute* or *subacute* (*serofibrinous, serohemorrhagic, puriform*) *pericarditis,* either with or without a high percentage of eosinophils, in addition to other hyperergic phenomena. If overlooked during its early stages, the effusion may follow a subacute or chronic course (simple chronic hydatid pericarditis). In such cases, the finding of hooklets in the fluid obtained by a pericardial tap is specifically diagnostic. Secondary *echinococcosis of the pericardium,* due to the vesicular transformation of scolices, may develop as a late complication of cystic rupture

Intramyocardial rupture of a fertile hydatid myocardial cyst may or may not be accom-

DIAGRAM 8-4 MECHANICAL ACCIDENTS DUE TO EMBOLIZATION OF HYDATID MATERIAL TO LEFT HEART CHAMBERS AND SYSTEMIC CIRCULATION



defensive reaction of the parasite aimed at assuring its survival. From this moment on, the hydatid cyst becomes multivesicular. Daughter cysts offer an identical constitution to that of the mother cyst and may suffer the same changes (degeneration, death, etc.). If intact, they can live and continue growing outside the mother vesicle after rupture of the latter.

The evolutive cycle of *Taenia echinococcus* is definitely closed when organs of intermediate hosts bearing fertile hydatid cysts are fed to dogs. In this way, thousands of scolices arrive at the intestinal mucosa of the animal, developing into the adult form of the parasite which, in the course of 4 weeks, reaches maturity. Besides this natural "major" cycle comprising two hosts, the parasite has a "minor" one, "taking place in a single host and depending on the process of the vesicular transformation of scolex" (Dévé, 1949). This minor cycle is commonly observed in man. Scolices contained in the primitive hydatid cyst may suffer the vesicular transformation (multivesicular cysts), and scolices liberated by rupture of the primitive cyst may undergo the same phenomenon in close contact with the cyst, in the relative vicinity, or at a distance, depending on the site of rupture of the cyst (secondary echinococcosis).

As far as human echinococcosis is concerned, the majority of modern authors agree with Dévé's statement that the *hydatid cyst of the heart is always primitive and single, even in cases where localizations other than cardiac are found* According to them, the hexacanth embryo, after passing through the capillary networks of the liver and lungs, arrives at the left heart chambers and reaches the coronary circulation, to become lodged finally in the interstitial tissue of any one of the four heart chambers or septa. Dévé (1946) also pointed out that the primary hydatid cyst is most frequently located in the wall of the left heart chambers (particularly the ventricle) rather than in the wall of the right, this fact is explained on the basis of a richer coronary circulation The authors' experience, based on observation of 18 cases, adds evidence confirming this conclusion (12 cases showed a left ventricular localization of the cyst)

Modern clinical and laboratory investigations in this field refute the old theory which maintained that cardiac hydatidosis was predominantly or exclusively secondary to the rupture of a primary hydatid cyst elsewhere in the human body and due to the grafting of the hexacanth embryo on the endocardial surface of the right heart chambers. From its original endocardial graft, the embryo would be able to reach any other region of the heart by active movements.

Jorge and Ré (1946) presented the theory that the hexacanth embryo can reach the heart via the lymphatic system (thus sparing the hepatic capillary network), based on the observation of many cases of cardiac echinococcosis with no concomitant hepatic cysts, on the bigger size of the hexacanth embryo if compared with that of the hepatic capillaries, and on the finding of ganglionary echinococcosis in some animals. They also accepted the possibility of transendocardial migration of the embryo once it had arrived in the right heart chambers.

Several authors state that cysts in the heart are found in about 0.5 to 2 per cent of the total cases of human echinococcosis.

An analysis of 35 cases in Uruguay (Larghero) shows that the incidence of cardiac echinococcosis is higher in the male than in the female (a ratio of 2:1). Statistics from other sources are in accordance with this proportion. Most cases were found in young persons (second to fifth decades) living in cattle-raising areas This is undoubtedly due to the close contact of persons with dogs harboring the parasites and an early human infestation.

PATHOLOGY; COMPLICATIONS

According to postmortem and surgical reports, the size of the primitive cyst of the heart varies between 1 and 15 cm in diameter

During its growth, the hydatid vesicle derived from the hexacanth embryo thins out the myocardial wall and exerts pressure on the surrounding muscle fibers, which become more or less ischemic, depending on the size of the parasite and on the resistance of the cardiac structures Because of mechanical, toxic, allergic, and inflammatory phenomena determined by the presence of the hydatid vesicle, the tissue reaction in the host leads to the formation of a fibrous capsule (enclosing the parasite) called *adventitia*, which shows cellular infiltration (mostly eosinophils) and which thickens gradually with the passing of time.

The development of the primary cyst in the myocardium is restrained by the particular density of the tissue and by functional elements This is more marked when it is located in either ventricle, particularly the left. Both

ferior vena cava Besides causing total or subtotal arterial occlusions, it is possible for embolized living daughter cysts to continue growing into vessels, causing *hydatid arterial aneurysms* and a *secondary intraarterial echinococcosis*. As they, in turn, may rupture into the vessels, further complications (mechanical or metastatic) can be expected after this accident.

Wide-open rupture of a primitive hydatid cyst (myocardial, pulmonary, hepatic) into the pericardial sac is responsible for different forms of *hydatid pericarditis*, depending on its contents (Diagram 8-5) If only ferble hydatid fluid comes into the pericardium (univesicular primitive cyst), an acute or subacute pericarditis may develop These forms may become chronic and purulent, if not diagnosed during their early stages Secondary echinococcosis of the pericardium represents the late complication of rupture of the cyst (univesicular primitive cyst).

Intrapericardial rupture of a multivesicular, altered primitive cyst may cause an acute, subacute, or chronic serofibrinous, puriform, or purulent *pericardial effusion* with hydatid material *in evolution* (living daughter cysts, free living scolices) or involution (entire "mother" membrane or fragments of it or dead daughter cysts) floating in it This complication, which must be named *hydatidopericardium*, originates a *hydatidopericarditis* Although a significant effusion (usually purulent) is almost always present, cases have been described with no effusion reabsorption?) Hydatidopericarditis may be generalized or localized (because of *pericardial adhesions*) It may also remain quiescent for a long time or produce cardiac compression or even be invasive Living daughter cysts contained in the pericardial effusion may be able to continue growing or may rupture into the pericardial sac or into a cardiac cavity, preferably into either atrium

Practically all forms of hydatid pericarditis (mostly, the chronic) cause a *thickening* of the pericardium *Constrictive pericarditis* has been found in cases of protracted evolution of an overlooked hydatidopericarditis (Larghero et al) Secondary cysts (pericardial grafts), as well as daughter cysts, may eventually rupture *into* the cardiac chambers, thus adding further complications to the original rupture of the primitive cyst.

CLINICAL PICTURE. DIAGNOSIS

The clinical picture of patients with echinococcosis of the heart varies considerably from case to case, depending upon the absence or presence of complications related to the rupture of the primitive hydatid myocardial cyst.

Most authors agree that "uncomplicated echinococcosis of the heart often remains silent and latent" and that it presents no particular clinical picture In some instances, nevertheless, patients may complain of cardiac symptoms (*palpitation*, *paroxysmal tachycardia*, *thoracic pains*, *precordial pain*, etc.).

We must recognize the fact that most cases bearing an intact hydatid myocardial cyst have been *discovered by roentgenologic examination* Mass chest x-ray examination has furnished several cases of this sort in Uruguay *Roentgenology* (fluoroscopy, roentgenograms, tomography, kymography) represent a diagnostic means of the highest importance in the detection of the disease, because the deformities of the cardiac silhouette and the calcifications may easily be discovered and studied in all projections These methods give sound information about the *size*, *shape*, and location of the abnormal mass, its *contour and movements*, and the location and magnitude of calcifications (Fig. 8-14A, B). Every shadow of calcific density projected *in* the periphery of the heart must evoke the possibility of a hydatid cyst, if signs of constrictive pericarditis are *not present* When spotty areas of calcification are seen in the cardiac shadow, one may also think of echinococcus *disease*, if calcification of the heart valves can be ruled out.

Angiocardiography may be helpful by giving information about the deformities imposed by the intramural development of a hydatid cyst on the internal outline of the cardiac chamber bearing it and about the thickness of the underlying myocardial wall (Fig 8-14C)

As has been emphasized in several publications by the authors, *electrocardiography* is a reliable diagnostic method in cases where the primitive hydatid cyst is located in the left ventricle. Compression ischemia of the myocardial fibers and thinning out of the ventricular wall caused by the hydatid cyst are expressed by a localized *ischemia patterns* and *changes in the QRS complexes* (reduced amplitude of R waves in some anterior or pos-

DIAGRAM 8-2. RUPTURE OF THE PRIMITIVE MYOCARDIAL HYDATID CYST INTO THE ENDOCARDIAL CAVITY

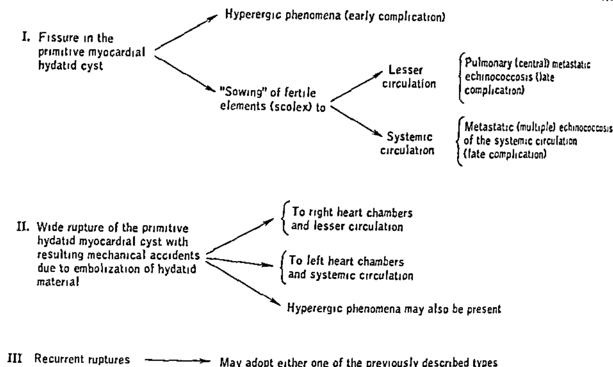
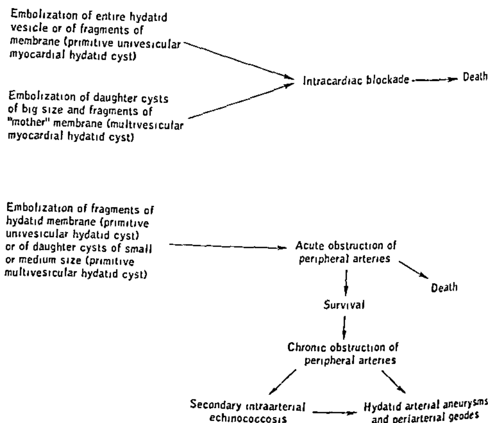


DIAGRAM 8-3 MECHANICAL ACCIDENTS DUE TO EMBOLIZATION OF HYDATID MATERIAL TO RIGHT HEART CHAMBERS AND LESSER CIRCULATION



The patient may remain symptom free for months and even years After this period of latency, he may present.

Signs or symptoms of chronic pericarditis (simple chronic hydatid pericarditis), chronic pericarditis with hydatid material floating in the effuson (hydatidopericarditis)

An enlarged and deformed cardiac silhouette (localized hydatidopericarditis, pseudo-aneurysmatic (invasive) form of hydatidopericarditis, secondary echinococcosis of the pericardium (pericardial grafts), usually combined with hydatidopericarditis]

Constrictive pericarditis (usually, an overlooked hydatidopericarditis leading to a marked thickening of both pericardial layers)

Multiple pulmonary secondary (metastatic) echinococcosis

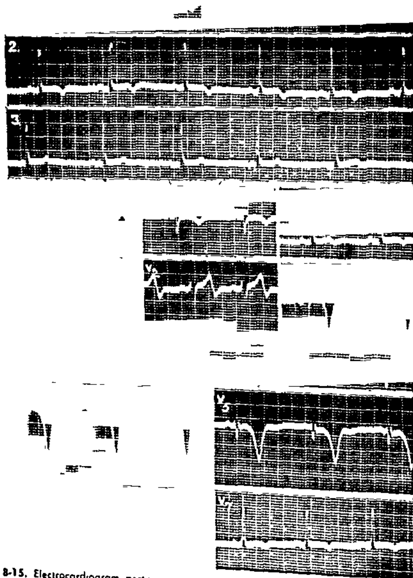


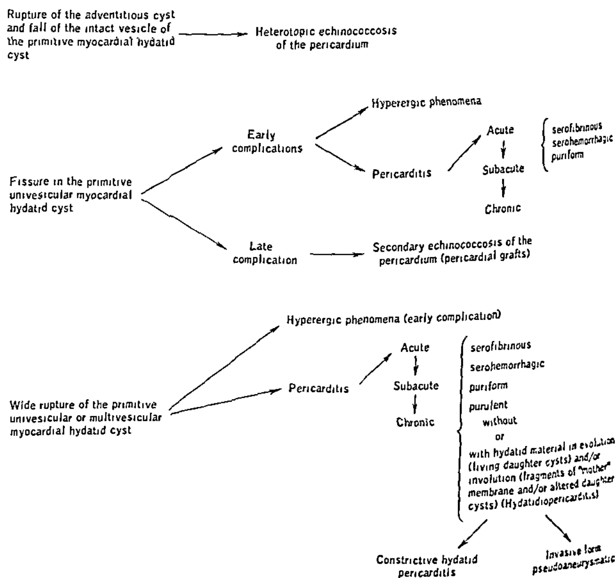
Fig 8-15. Electrocardiogram pertaining to a case of myocardial hydatid cyst located in the apical region of the left ventricle (same case as that of Fig 8-14C). Coronary-type inversion of T waves may be seen in different leads. Changes in the QRS complexes are present in several precordial leads (mostly in V_3, V_4, and V_5).

panied by hyperergic phenomena. Its late complication (*local secondary intramyocardial echinococcosis*), which has often been wrongly interpreted as multiple primitive hydatid cysts of the heart, was described by Dévé as follows:

> A group of independent and contiguous cysts developed in close contact with an older pouch, often in involution. The number of cysts may be between 2 and 12, their size varying between that of a pea and that of a grape. Some cysts seem to be located in the myocardium proper, most of them being situated subendocardially. At times, they form a pediculated tumor submerging into the cardiac cavity. This polycystic lesion is usually associated with multiple cysts developed at a distance in organs located "downstream."

If an ample rupture of the primitive myocardial cyst occurs into the lumen of the chamber bearing it (Diagrams 8-2 to 8-4), two different kinds of complications may appear, the immediate ones, represented by the hyperergic phenomena just described, and the late ones. Late complications, besides *metastatic echinococossis* of the lesser or systemic circulation, are caused by *embolization* due to the entire membrane of the primitive cyst or its fragments, to daughter cysts (living or dead, if the cyst is multivesicular), or to hydatid debris, which lodge in vessels of the lesser (*hydatid cor pulmonale*) or systemic circulation. These complications may also be immediate Sudden death occurs in some cases right after rupture of the hydatid cyst into the endocardial cavity owing to *intracardiac bloockade* or *pulmonary* or *cerebral embolism*. This may also happen in cases of hepatic cysts rupturing into the in-

Diagram 8-5. Intrapericardial Rupture of the Primitive Myocardial Hydatid Cyst



possible way of treating echinococcosis of the heart with a *reasonable margin of safety and success.*

Surgical approach must be conducted through a *wide incision* made along the *left* 5th intercostal space. Rib resection can *be avoided by using* the chondrosternal disjunction technique. Removal of a *fertile* univesicular hydatid cyst from the myocardium must be *done with extreme caution in* order *to prevent* the spilling of hydatid fluid in the operative field. Puncture and aspiration of the hydatid vesicle *through* a *needle must be carried out carefully.* Thereafter, the use of a parasiticide is *mandatory (saturated saline solution* is the best, *other parasiticides such as* Formalin and ether being dangerous for the myocardium) Removal *of the hydatid ("mother")* membrane is the *following* step after incision of the adventitious cyst and washing of the cystic cavity with saline.

If the primitive hydatid cyst is located in either atrium, the entire cyst *(hydatid vesicle plus adventitious* cyst) and the region of the *atrial* wall in which the cyst is grounded can be removed at once, if anatomic conditions *allow it (Crafoord, 1953). This technique cannot be applied* to cases of ventricular cysts. The surgeon, after evacuating the hydatid material of the cyst, can *proceed to resect only* the bulging portion of the adventitious cyst. *In order* to prevent *cardiac aneurysm, the ventricular* wall must be *reinforced,* if the cyst has thinned out the myocardium to any great extent.

In cases of intrapericardial rupture of a hydatid cyst, *the surgeon must deal with* the *myocardial cyst* proper after evacuating the pericardial effusion and the hydatid material (daughter *cysts, fragments of "mother"* membrane, etc.) shed into the pericardial sac. This surgical procedure *may prevent or* delay the *appearance of further* complications (Diagram 8-5).



Fig. 8-14. A. Roentgenogram showing a calcified myocardial hydatid cyst located at the apical region of the left ventricle. B. Tomographic study of a case with an altered hydatid cyst located at the high lateral region of the left ventricle. Stratified calcifications are present. C. Angiocardiographic study of a case of hydatid cyst of the left ventricle having thinned out the myocardial wall. Amputation of the internal outline of the cardiac chamber is present.

terior chest leads). Atrial cysts may or may not alter the P waves. In septal cysts, abnormalities have been noticeable in the P-R interval and QRS complexes (notching, slurring) (Figs. 8-15 and 8-16).

Some special laboratory examinations must be carried out in every possible case of cardiac echinococcosis. An *eosinophil count* of 7 per cent and above may be of significance. Eosinophilia may be absent in old, altered, and even intact cysts. The *intradermal Casoni test*, if positive (best, if late positive), is of diagnostic value. Emphasis must be laid on the fact that well-documented cases of this disease have repeatedly shown negative intradermal tests. Neither are *complement-fixation tests* (Weinberg, Ghedini) entirely specific. reactions for the diagnosis of this condition may often be discordant.

Rupture of the primitive myocardial cyst usually alters the "symptomless" period of echinococcus disease of the heart Depending on the contents and on the site and type of rupture (see diagrams), different signs and symptoms may appear immediately after or may appear later on (hours, days, weeks, or years).

The patient may die suddenly because of:

Anaphylactic shock.

Intracardiac blockade, if big fragments of the "mother" membrane or large-sized daughter cysts are released into the cavities of the heart

Acute cor pulmonale, caused by embolization of fragments of "mother" membrane or living or dead daughter cysts in the lesser circulation, if rupture of the cyst takes place into either of the right heart chambers.

Embolization of hydatid material to the *cerebral circulation*, if the cyst ruptures into either one of the left heart chambers

Hemopericardium.

The patient may survive the initial anaphylactic shock Different clinical pictures may develop thereafter:

An acute or subacute pericarditis (serofibrinous, serohemorrhagic, or puriform effusion with or without high percentage of eosinophils and hooklets) may appear hours or days after the anaphylactic shock

The patient may show early evidence of *acute cor pulmonale* or of *cerebral* or *peripheral arterial embolism.*

trypanosoma which had not yet been described in the literature and which Chagas named *Trypanosoma cruzi*.

Considering the habits of these triatomid insects [illegible] and the number of patients pre- [illegible]

[illegible] anosoma in the blood of a feverish child, [illegible] house he had previously discovered the same microorganism in the blood of a diseased cat.

Afterwards, having as collaborators Gaspar Vianna, Artur Neiva, Eurico Villela, and Magarinos Torres, he collected numerous data which proved that *T. cruzi* was responsible for a morbid entity, which was later named Chagas' disease.

At the time of Chagas' death (1934), Chagas' disease was well known. Although the disease became widely known, and isolated cases were described in various countries of the American continent, interest in it outside Brazil became widespread only after the work of Mazza et al. (1934).

Geographic Distribution. Except for the Dutch and British Guianas, Chagas' disease has been reported in every American country (Fig. 8-17). There has been, however, no proved case of Chagas' disease in human beings outside the American continent. Natural infection by *T. cruzi* in Asiatic monkeys has been reported by various investigators. In tropical Africa, India, French Indo-China, New Guinea, and the Malayan States, some species of triatomid bugs have been described. In the Southwest of the United States (California, Arizona, New Mexico, and Texas) the percentage of triatomas naturally infected by *T. cruzi*, as studied by various investigators, averages 20 per cent, a figure similar to that of the regions of Brazil where the disease is endemic. [illegible] there has been only one proved case [illegible]

On the other hand, little has been done in order to determine the actual prevalence of Chagas' disease. Data collected in Argentina, Brazil, Chile, Uruguay, and Venezuela (Table 8-3) show the dissemination and the importance of the disease in these countries.

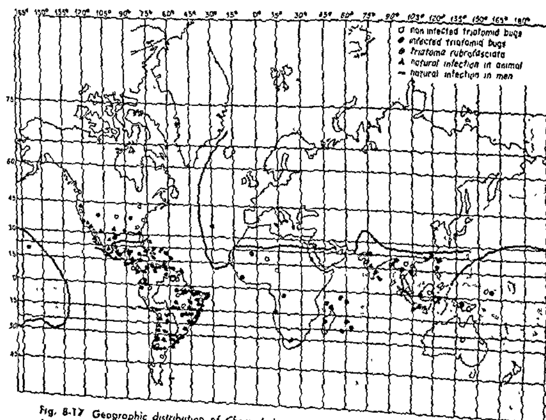


Fig. 8-17 Geographic distribution of Chagas' disease. (Adapted from various authors by Prof. J. L. Pedreira de Freitas, 1958.)

Chronic cor pulmonale with or without metastatic pulmonary echinococcosis

Multiple (metastatic) echinococcosis of the systemic circulation (cerebral, renal, splenic, muscular, etc.)

The patient may come to consultation with one or several of the above-mentioned complications and without a clear-cut history of previous anaphylactic shock. Sometimes etiologic diagnosis in such cases is quite difficult.

DIFFERENTIAL DIAGNOSIS

As the primitive hydatid myocardial cyst usually produces a localized deformity in the cardiac outline, this condition may be confused with pericardial cysts and diverticula, mediastinal tumors and cysts in close contact with the heart, cardiac tumors, cardiac aneurysms, etc.

A *peripheral rim of calcification* in the abnormal bulge is practically pathognomonic of the disease *Spotty areas of calcification* are also of diagnostic significance, as well as a marked blood eosinophili, a positive Casoni test, and a positive complement-fixation test (Weinberg reaction).

A normal ECG negates the diagnosis of hydatid myocardial cyst, except in cases of atrial localization A left ventricular hydatid cyst produces electrocardiographic and angiocardiographic changes distinct from those due to a cardiac aneurysm, as has been emphasized by the authors

If an intact hydatid cyst is suspected as the cause of a *localized cardiac deformity*, under no circumstances should puncture of the abnormal bulge be attempted.

Intrapericardial rupture of the primitive hydatid cyst can obscure the diagnosis of the disease, if the accident is not accompanied by an anaphylactic shock. In such cases, a pericardial tap may be diagnostic, by showing pericardial fluid containing a high percentage of eosinophils, hydatid hooklets, or both.

Bizarre (polycyclic, pseudoaneurysmatic, etc.) outlines of an enlarged cardiac silhouette may be seen in cases of hydatidopericarditis (localized or generalized) or pericardial hydatid grafts.

Multiple pulmonary cysts (best, if bilateral), besides a localized cardiac bulge, may prove an old rupture of a hydatid myocardial cyst in the right heart chambers

PROGNOSIS

The authors have stated that "diagnosis of hydatid disease of the heart must be made in the early, uncomplicated stages of the disease, prior to the occurrence of any one of its common and dreaded complications If not so, there remains little or nothing to be done for the benefit of patients in most cases" Diagrams 8-1 to 8-5 give an approximate idea of what can happen to the patient whose cardiac echinococcosis is diagnosed in the late, complicated stages of the disease.

TREATMENT

In the absence of serious extension of the disease (see diagrams), surgery is the only

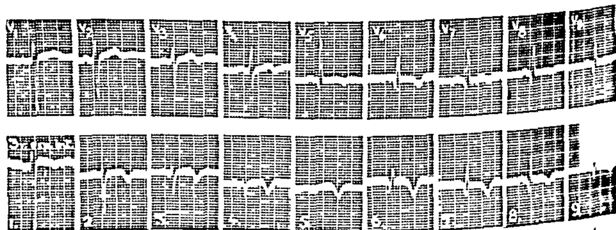


Fig. 8-16 Comparative electrocardiographic study between "standard" precordial leads and leads taken at the level of the 3d intercostal space. Changes in QRS complexes and T waves are more marked in the latter, in strict correspondence with the position of the myocardial cyst (high lateral region of left ventricle)

mucosa is a *frequent site* of entrance of the parasite, transmission is not possible *through* the normal skin. Transmission through a bite *has been accomplished* experimentally with difficulty and must be considered exceptional, since the infectious forms are *found in the hind* gut. When it occurs, it seems caused by either *regurgitation of gastric* content or contamination of the sting by feces.

Congenital transmission, suspected by Chagas (1911), was observed in animals by various ... It was demonstrated in man by

... was *reported* by Nattan-Larrier ... in the guinea pig and observed by Mazza et al. (1936) in human beings. Transmission through blood transfusion was proved by Freitas et al. (1952) *in man*

Various exceptional mechanisms of transmission have been described, as when an animal eats the triatomid insect or when an infected *animal is ingested, thus causing transmission through the digestive* tract

Pathogenesis. After penetrating the cells at the site of inoculation, the trypanosomas *change to leishmanias, which multiply* by successive binary fission, forming pseudocysts. Experimental studies support the view that there is no inflammatory reaction at the site of inoculation *before the infected cell ruptures.* This occurs from 4 to 5 days after inoculation. Then, the parasites enter into the blood stream as trypanosomas, invading all organs and tissues.

In the cardiac cells, the protozoon, under the form of leishmania, divides by successive binary fission (Vianna, 1911). The fiber probably ruptures by mechanical action of the parasitized *corpuscles over* the sarcolemma (Torres, 1917). The leishmania forms, which have not reached the trypanosoma stage, are caught and destroyed by the macrophages when they are *in the interstitial spaces.*

Torres (1942) observed that the *inflammatory reaction* begins in the capillary vessels of the parasitized site. These vessels show some tumefaction and marginal *deposition of the leucocytes, followed* by migration of monocytes to *the interstitial* tissue. Capillary constriction, with consequent collapse of the vessel wall, causing approximation of the endothelial cells, was also observed *He postulated that these lesions might be* caused by an allergic reaction *of the organism*, which is already sensitized.

Muniz and Azevedo (1947) were able to sensitize rhesus monkeys with lysate and *suspension* of dead forms of cultured *T. cruzi,* free from foreign *proteins*. With further inoculation they produced, 12 days later, *the typical histopathologic* picture of the Chagasic myo*carditis.* On the other hand, the inoculation failed to produce the same picture when made *in nonsensitized animals.*

... (1958) considers that the inflamma- ...

... a relative *stimulation* of the sympathetic nervous system, resulting from partial or total vagal paralysis. Cardiac action occurring in such conditions would be followed by dilatation and hypertrophy of the heart.

The degenerative lesions of the cardiac fibers were considered by Andrade and Andrade (1955) as due to *ischemia, chiefly caused by* the destruction of small vessels, resulting from ...

... tive coronary insufficiency.

The inflammatory process goes on continuously *and progressively* but becomes gradually less severe while, at the same time, areas of disseminated fibrosis develop. The inflammatory process *of the myocardium, according* to Torres (1928), may cause *mural thrombi,* generally in the endocardium of the left ventricle (apex), right atrium, and right auricular appendage. These thrombi may give origin to emboli, which then block vessels of either the pulmonary or the systemic circulation (Figs. 8-19 and 8-20).

Pathologic Anatomy. ACUTE CHAGAS' DISEASE. During the initial stage of the infection, the protozoons have been observed in almost every organ, where they *multiply as leishmania forms*

Upon gross examination, the involved heart presents global dilatation and flattens when left on a surface. Pericardial exudate *may be found* occasionally (Chagas, 1916a).

Microscopically, intense inflammatory changes in the interstitial tissues are seen to produce the picture of an *infiltrate* of monocytes, histiocytes, lymphocytes, and plasmacytes; *within* the muscle fibers dissociated by

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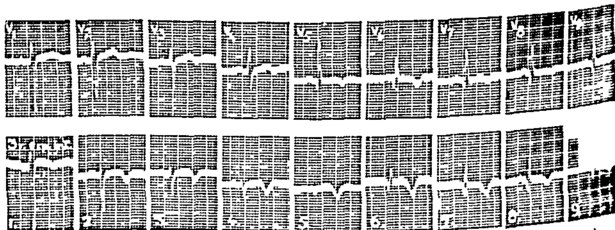


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Koberle (1958) considers that the inflammatory reaction is caused by the destroyed parasites. This inflammation propagates along the interstitial tissues, reaching the intramural nervous cells. He points out that the destroyed parasites liberate a toxic substance which causes degeneration of the neurons. This would cause a relative stimulation of the sympathetic nervous system, resulting from partial or total vagal paralysis Cardiac action occurring in such conditions would be followed by dilatation and hypertrophy of the heart.

The degenerative lesions of the cardiac fibers were considered by Andrade and Andrade (1955) as due to ischemia, chiefly caused by the destruction of small vessels, resulting from the reactivation of a subacute focus. Koberle (1958) admitted the ischemic nature of these lesions as a result of hypoxia, secondary to relative coronary insufficiency.

The inflammatory process goes on continuously and progressively but becomes gradually less severe while, at the same time, areas of disseminated fibrosis develop. The inflammatory process of the myocardium, according to Torres (1928), may cause mural thrombi, generally in the endocardium of the left ventricle (apex), right atrium, and right auricular appendage. These thrombi may give origin to emboli, which then block vessels of either the pulmonary or the systemic circulation (Figs. 8-19 and 8-20).

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Parasitic heart diseases

ADAUTO BARBOSA LIMA AND ANIS RASSI

The parasitic heart diseases may be divided into two main groups:

1. *Protozoal*
   a. Trypanosomiasis
   b. Amebiasis
   c. Malaria
   d. Leishmaniasis
   e. Toxoplasmosis
   f. Sarcosporidiosis
2. *Helminthic*
   a. Trichinosis
   b Strongyloidiasis
   c. Filariasis
   d Schistosomiasis
   e Echinococcosis

Both groups show cardiac changes which may either result from the direct action of the agent or be secondary to changes caused by the parasite in another organ. In cardiology, the importance of each disease is related to the endemic area of the infection, and the severity and frequency of heart involvement.

TABLE 8-3 INFECTION PREVALENCE BY TRYPANOSOMA CRUZI IN UNSELECTED POPULATION FROM ENDEMIC AREAS

Country	*No. of persons examined*	*Percentage of infection*	*Author*
Argentina	3,071	19 7	Romana, 1954
Brazil	979	54 9	Ramos et al , 1949
Brazil	3,176	20 02	Unti and Silva, 1952
Brazil	1,394	31.92	Brant et al , 1955
Chile.	10,666	14.25	Neghme et al , 1949

Although cardiac lesions may be found in trypanosomiasis caused by *Trypanosoma gambiense* and *T. rhodesiense* (African trypanosomiasis), they are not important features of the disease On the other hand, *Chagas' disease* (South American trypanosomiasis), caused by *T. cruzi,* is the most important entity in this group, judging by the size of the endemic areas and the number of individuals affected In fact, it has become one of the major problems of the American countries (Table 8-3, Fig. 8-17).

The possibility of transmission of the infection by blood transfusion is another important aspect of the problem that may interest physicians from countries where the disease is uncommon or does not exist

CHAGAS' DISEASE

Chagas' disease is a generalized protozoan infection caused by *Trypanosoma cruzi* (Chagas, 1909)

History. Having been appointed to supervise a campaign of malarial control in the state of Minas Gerais, Brazil, Carlos Chagas soon found that another disease was common in that region, where the huts were infested by hematophagous insects ("kissing bugs," locally called *barbeiros*).

Knowing the importance of these insects as vectors of various diseases, Chagas searched for microorganisms in their intestinal tracts and found many flagellates with the morphologic characteristics of the crithidias At his request, Oswaldo Cruz, eminent Brazilian health officer, tried to infect monkeys (*Callithrix penicillata*). Twenty to thirty days thereafter he was able to identify a

A

B

Fig. 8-20. A. Apical atrophic lesion of the left ventricle free of thrombus. (Courtesy of Prof. C. Mignone.) B. Thinness of the tip of the heart. Sagittal view of the left ventricle. (Courtesy of Prof F. Koberle.)

almost diagnostic of chronic Chagas' myocarditis.

The major coronary artery branches usually show dissociation of every layer. The arterioles and the venules may present slight and inconstant inflammatory changes.

During the chronic phase, fibrosis is the dominant picture in the conducting system, with destruction of the fibers and slight mononuclear infiltration of the interstitial tissue (Torres and Duarte, 1950).

No organic lesions of the valves have been demonstrated in man.

Clinical Picture. Since his initial studies, Chagas (1911) recognized two clinical pictures, acute and chronic. The scarcity of acute cases reported in the literature, compared with the frequency of the chronic forms, might be explained by the mild symptoms or by the fact that the signs of infection are not recognized by the patient or even by the doctor.

ACUTE CHAGAS' DISEASE. It takes about 10 days after the inoculation for the appearance of signs The acute stage is more commonly found in children who have been exposed to the infection since birth (Chagas, 1916a). In the summer, the triatomid insects are more active, consequently the acute cases become more frequent. The portal of entry of the parasite may be recognized in about 50 per cent of patients by the eye's sign (Fig 8-22A), in 25 per cent by the cutaneous chagoma, while in the remaining 25 per cent, it is not apparent. The higher percentage of cases in which the



Fig. 8-21. Leishmania forms of *Trypanosoma cruzi* in the myocardium. (Courtesy of Prof. W. E. Maffei)

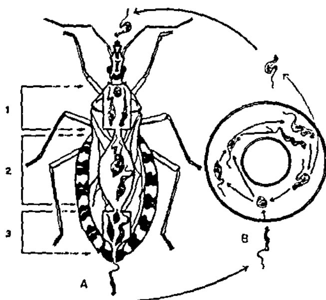


Fig. 8-18. Life cycle of *Trypanosoma cruzi.* Developmental forms. A. Invertebrate host: 1, stomach—leishmania, crithidia, trypanosome; 2, midgut—crithidia forms; 3, hindgut—free and adherent crithidias, metacyclic trypanosomes. B. Vertebrate host: in the tissues—leishmania, crithidias; in the blood—trypanosomes.

The Etiologic Agent and Its Life Cycle

Chagas' disease is caused by *T. cruzi* (Chagas, 1909), a protozoon of the class Mastigophora. The life cycle of *T. cruzi* has two stages, one in man or other vertebrate, and one in the transmitting insect (Fig. 8-18). In the vertebrate, the typical trypanosoma form is found in the blood and the leishmania form in the tissue cells The typical trypanosoma form, as found in the blood of the vertebrate, may be ingested by the transmitting insect and passes along its intestinal tract through various developmental stages, evolving to the metacyclic trypanosoma (infectious form) only when the rectum is reached. Reproduction is by binary fission of the crithidia forms in the midgut This stage lasts from 8 to 10 days

The metacyclic *trypanosomas* found in the feces are infectious to both man and animals. They penetrate the interior of the cells through the normal mucosa or through a skin lesion. They lose their flagella and undulating membranes at the site of inoculation, thus becoming *leishmanias*

The leishmania form divides by successive binary fission, which results in the formation of *pseudocysts.* After about 5 days, the leishmania form evolves to a trypanosoma, which, after rupture of the infected cell, enters the blood stream The circulating trypanosoma penetrates again into a cell, again becoming a leishmania, and the cycle repeats again.

PROTOZOAN RESERVOIR. Various domestic and wild animals have been found infected with *T. cruzi.* As the triatomid insects are well adapted to human dwellings, it is obvious that both man and domestic animals are most important epidemiologic reservoirs Freitas (1950) examined 563 dogs and 492 cats (65 per cent of the local dog and cat population) in a heavily endemic area of Brazil, and proved the infection in 28 6 per cent of the dogs and 19.7 per cent of the cats. In the United States, various animals are naturally infected by *T. cruzi:* armadillos (*Dasypus novemcinctus*), opossums (*Didelphis virginiana*), house mice (*Mus musculus*), and wood rats (*Neotoma micropus micropus*).

EXPERIMENTAL INFECTION. The most suitable animals for laboratory studies are the dog, cat, mouse, and guinea pig, which are most sensitive to the infection, chiefly when young It has been observed that birds, reptiles, and batrachia are refractory to this infection.

INSECT VECTORS. The infection is transmitted from man to man or from animal to man by Hemiptera insects belonging to the family Reduviidae, subfamily Triatominae. About 100 species have been found in the American continent from Utah to San Luis (Argentina). Outside the American continent, approximately 10 species have been reported, but none has been naturally infected by *T. cruzi.* In general, one species is more common in a certain region. In South America, the most important species are *Triatoma infestans, Rhodnius prolixus,* and *Panstrongylus megistus* In Central America and Mexico, the *Triatoma pallidipennis, Triatoma phyllosoma,* and the *Triatoma dimidiata* are the most common. Natural infection in triatomids has been described in about 40 species.

The triatomid insects adapted to human dwellings are generally found in huts made of mud They live in the cracks of the walls and behind pictures. They come out after dark and usually bite uncovered parts of the body. Their bite is painless and does not awaken the victim. These insects are exclusively hematophagous and their activity is greater in summer. The percentage of infected triatomid insects varies from 20 to 40 per cent in surveys from several large endemic areas.

TRANSMISSION Transmission of *T. cruzi* usually occurs by contamination, through rubbing of the feces of the triatomid insects, rich in metacyclic trypanosomas, on skin abrasions caused by itching or through bite. The normal

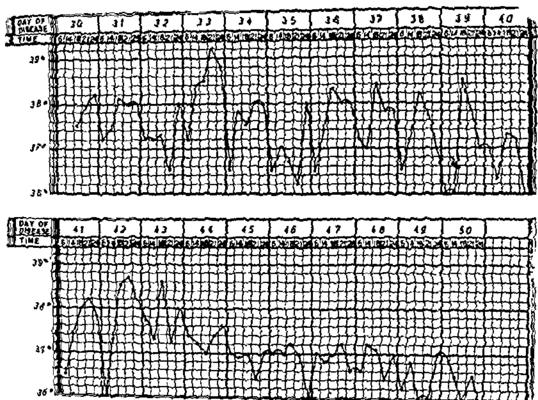


Fig. 8-23. Acute Chagas' disease Temperature chart of a 15-year-old patient.

"puffy" appearance similar to that of patients with nephritis. It disappears spontaneously together with the other symptoms.

Lymph node enlargement is a common manifestation which may persist for several months. The nodes become hypertrophied and firm, they are not adherent and are painless.

Moderate *hepatosplenomegaly*, generally accompanied by tenderness, is frequent Diarrhea and vomitus, cutaneous rash (schizotrypanides, Mazza et al, 1941), and meningoencephalitis may be observed.

Although the circulatory system shows pathologic changes in almost every case, the involvement is not always accompanied by clinical, radiologic, or electrocardiographic signs On account of the temporary aspect of certain manifestations, it is important to repeat the examinations at short intervals, particularly the roentgenographic and electrocardiographic ones (Figs 8-24 and 8-25)

Chagas (1916*i*) called attention to the *hypotension*, the *tachycardia* (which is out of proportion to the fever), and a slight *cardiac enlargement*, usually accompanied by *pericardial effusion*. Heart failure, when present, has no typical aspects. Arrhythmias are not frequent in the acute stage.

Radiologic findings. Cardiac enlargement was found in 86 per cent of 61 cases (Aguirre and Gimenez, 1939). It is usually global, but is occasionally limited to the left chambers. Various degrees of enlargement, from slight to accentuated, may be observed (Fig. 8-25).

Electrocardiographic Findings The most common electrocardiographic findings are sinus tachycardia, low voltage of the QRS complex, prolongation of the P-R interval, and primary T-wave changes Ventricular extrasystoles are less frequent. Intraventricular block and S-T changes are exceptional and found only in severe cases. On the other hand, the electrocardiogram is often normal. Laranja et al. (1956) observed normal electrocardiograms in 56 7 per cent in a series of 180 cases.

The electrocardiographic and radiologic changes are transient and may last from a couple of weeks to several months, with complete normalization occurring thereafter (Figs 8-24 to 8-27)

Laboratory Findings. Leucocytosis is frequent, but sometimes the white blood count

edema, where leishmania forms are easily identified, waxy and fatty degeneration of the cardiac fibers are most commonly seen (Fig. 8-21). Köberle (1958) described the intense degeneration of the nerve fibers of the heart, which he considered as the most important *histologic finding*.

The lesions of the conducting system of the heart in the acute phase are characterized by mononuclear infiltration of the *interstitial tissue*, producing compression of muscle fibers. These are accentuated in the AV node and in the first portion of the right stem of the bundle of His (Torres and Duarte, 1950). In the acute stage, according to Vianna (1911), an invasion of neuroglia by the *T. cruzi* forms nidi, which rupture and produce an *inflammatory process*.

CHRONIC CHAGAS' DISEASE The heart shows severe enlargement with a global shape on account of dilatation and hypertrophy of its chambers. Its average weight is 500 Gm (Andrade and Andrade, 1955).

Microscopically, fibrotic degenerative lesions result from ischemic changes and reactivation of inflammatory foci. This inflammatory reactivation shows a predominance of lymphocytes over the monocytes as the lesion becomes older. Various degrees of fiber degeneration are seen, resulting in *atrophy* and *necrosis*. Parasites (Fig. 8-21) are not easily found; they are observed more often in the right atrium (Köberle, 1958). Pathologic changes are seen also in the endocardium, pericardium, and the specific conducting system. All chambers are equally involved, but, on account of its thin wall, the *right ventricle often shows a relatively greater damage*. This may explain the usual clinical picture of right ventricular failure, without previous evidence of left ventricular failure (Mignone, 1958).

Parietal thrombosis is more often found in the endocardium at the apex of the left ventricle, in the right atrium, and in the right auricular appendage (Fig. 8-19). Fragments of these thrombi are easily freed and are an important source of *emboli*, which may reach either the pulmonic or the systemic circulation. The tip of the left ventricle may show a fibrotic degeneration, becoming soft and very thin. *Slight aneurysmatic dilatation* at this site was observed in 45 per cent of 124 cases (Mignone, 1958). According to this author, this sign is



Fig. 8-19. A Apical lesion of the left ventricle occupied by an organized thrombus. B. Apical lesion of the left ventricle partially occupied by thrombus (Courtesy of Prof. C. Mignone.)

has to be distinguished from various ocular disturbances conjunctivitis of different types, trauma, Quincke's edema, cellulitis of the orbit, other insect bites, myiasis, etc. A history of having been bitten by triatomid insects helps in the identification of the etiologic agent.

Many diseases may produce a clinical picture similar to the general manifestations of acute

laria, and acute glomerulonephritis. When, in the acute stage, there is evidence of meningo-encephalitis, other etiologic factors have to be discussed If there is cardiac involvement, rheumatic heart disease and bacterial endocarditis must also be considered in the differential diagnosis.

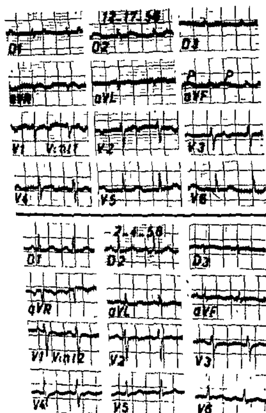


Fig 8-26 Acute Chagas' disease The first tracing (12/17/56) shows a prolonged P-R interval The P wave is fused with the preceding T wave Fourteen months later (2/4/58): Normal sinus rhythm with increased voltage of QRS complex in all leads (the precordial leads were taken with normal standard in the first tracing and with half-standard in the second).

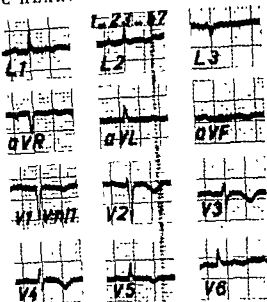


Fig. 8-27. Acute Chagas' disease. In the first tracing (1/23/57), ÂT is oriented to 108°. Note the negative T waves in all leads except AVR and AVL, demonstrating a diffuse subepicardial ischemia, as seen in pericarditis The second tracing (5/17/58) shows normalization of the T waves

CHRONIC CHAGAS' DISEASE. After the acute stage, the patient becomes apparently normal for a long period, which varies from 10 to 20 years (Laranja et al, 1956) Nothing is known about the course of the disease during this interval, when the diagnosis can be made only by means of laboratory tests.

In the endemic areas, Chagas' disease is the most frequent etiologic factor of heart disease,

edema, where leishmania forms are easily identified, waxy and fatty degeneration of the cardiac fibers are most commonly seen (Fig. 8-21). Koberle (1958) described the intense degeneration of the nerve fibers of the heart, which he considered as the most important histologic finding.

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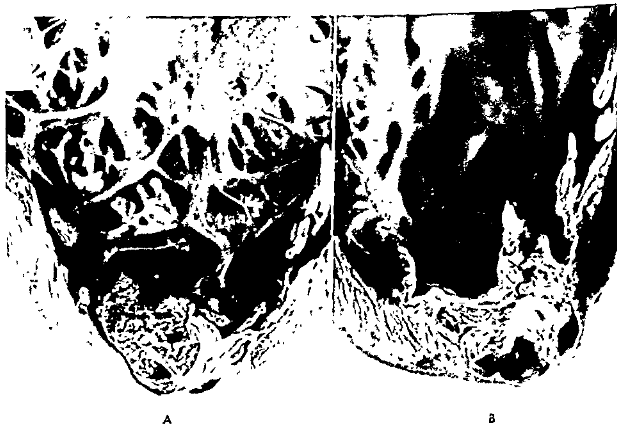


Fig. 8-19. A. Apical lesion of the left ventricle occupied by an organized thrombus. B. Apical lesion of the left ventricle partially occupied by thrombus (Courtesy of Prof. C. Mignone)

be accentuated by effort and is frequently reported by patients as the chief complaint.

In the medical centers where patients from the endemic areas are observed, one of the most frequent causes of heart disease is the chronic stage of Chagas' disease (10.81 per cent—Tranchesi et al., 1951; 12.5 per cent—Tabacof, 1954).

Chagas (1916a) suggested some relationship between Chagas' *disease* and *dysphagia*. Several investigators have observed a high incidence of megaesophagus and megacolon in areas where Chagas' disease is endemic. The finding of 90 per cent of positive *Guerreiro-Machado reaction* in patients with megaesophagus or megacolon led the authors to accept Chagas' disease as its etiologic agent. This figure is undoubtedly higher than the findings of surveys made in unselected persons from the endemic areas. Koberle and Nador (1955) claim to have demonstrated the "specific" nature of the inflammatory process in the esophageal musculature, similar to the myocardial process, and suggest that the symptoms might be explained by the destruction of Auerbach's plexus and Meissner's plexus.

Physical Examination. Runs of *extrasystoles* are frequently present and often elicited by exertion. Isolated extrasystoles or bigeminal extrasystoles are also frequent. A *split 2d pulmonic sound* and a *weak 1st heart sound at the apex* are common. A high-pitched, soft *systolic murmur* is commonly heard at the apex. Triple rhythm is less frequent. It is not rare to observe patients with severe cardiac enlargement in

TABLE 8-4. CARDIAC AREA AT X-RAY IN 387 CASES OF CHRONIC CHAGAS' HEART DISEASE

Condition	No. of cases
Normal	182
Cardiac enlargement:	
Slight	64
Moderate	55
Accentuated	86

spite of the lack of symptoms. The blood pressure may be normal or show a decreased systolic level.

Embolic manifestations involving the lungs, brain, kidneys, and spleen are frequent. They are caused by mural thrombi of the left ventricle (Nussenzveig et al., 1953, Andrade and Andrade, 1955).

X-ray Findings. The heart size is normal in a great number of cases. Slight, moderate, and severe enlargement are observed (Table 8-4). Enlargement is usually due to dilatation of all cavities. Faint pulsations are observed. Great *dilatation* of the right atrium and ventricle, associated with clear peripheral lung fields, is frequent (Fig. 8-29). Right heart failure usually predominates over left heart failure. This explains the absence of radiologic signs of the latter.

Electrocardiographic Findings (Table 8-5). The electrocardiogram is one of the most valuable methods for the diagnosis of chronic Chagas' heart disease. Many asymptomatic patients, without physical signs or radiologic changes, have an abnormal electrocardiogram suggesting Chagas' heart disease.

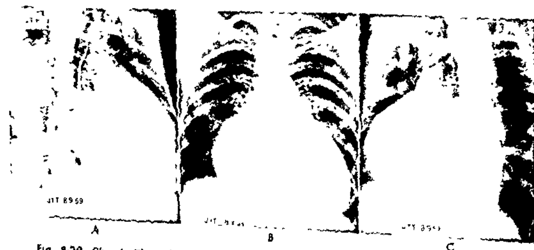


Fig. 8-29. Chronic Chagas' disease. Great heart enlargement with signs of all heart cavities. Lungs are clear

site of entry is indicated by the eye's sign may be explained by the fact that this sign is easier to recognize. Also called Romaña's sign (1935), it consists of an elastic and painless unilateral edema of the eyelids, which assume a violet-pink color. The conjunctiva becomes congested, and there is a satellite reaction of the preauricular, parotid, and submaxillary nodules. The sign disappears spontaneously after 1 to 2 months.

The *chagoma* is characterized by a slight cutaneous bulge, which is hard, reddish, slightly painful, and surrounded by an elastic edema. It is also followed by a nodular satellite reaction, and sometimes becomes ulcerated (Fig. 8-22B). It may appear in any part of the body but is more common in the uncovered part. It heals spontaneously in about 1 to 2 months, and leaves in its place a slight pigmentation.

Signs and Symptoms. The acute phase is accompanied at first by general malaise, fever, headache, and weakness. Fever is present in almost every case but is more severe in infants and children (Fig. 8-23). In the first days of the disease, a pattern of *continuous or recurrent fever* is most commonly seen, although this pattern may vary. The fever lasts from 4 to 5 weeks; the return of the temperature to normal is gradual.

Edema appears around the second week, showing an elastic consistency (Chagas, 1916a). It may be generalized or localized in the extremities or in the face, producing a

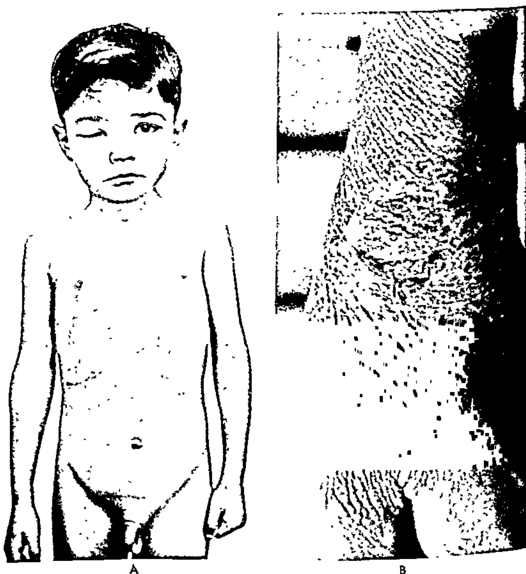


Fig. 8-22. A "Eye sign," also known as "Romaña's sign," used in diagnosis of Chagas' disease. B. Epidermic chagoma (ulcerated).

Chagas' disease. The common electrocardiographic findings are a small QRS complex, frequent extrasystoles, and RBBB (Figs. 8-31 and 8-33); their association with the radiologic findings of right atrial and ventricular enlargement in the presence of clear lung fields (Fig. 8-29) makes differentiation from Ebstein's disease difficult (Barbosa Lima et al., 1957). The association of RBBB with superiorly oriented AQRS is more frequent in chronic Chagas' heart disease than in Ebstein's disease. However, the fact that any other cardiac disease

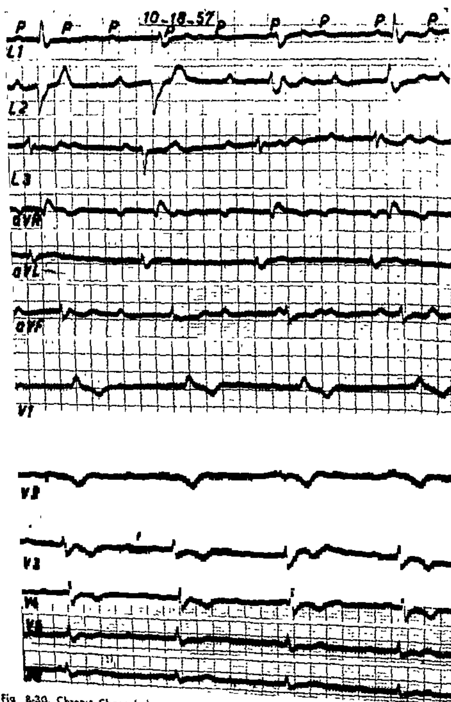


Fig 8-30. Chronic Chagas' disease, 10/18/57. Complete AV block. Idioventricular rhythm of multifocal origin (L_1, L_2, L_3).

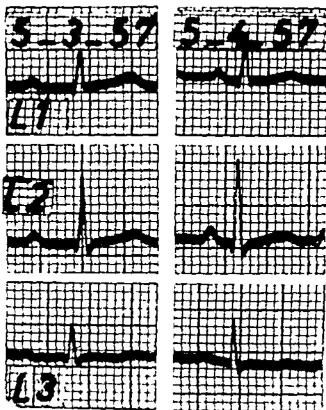


Fig. 8-24. Acute Chagas' disease. Prolonged AV conduction (P-R interval, 0.24 sec) with normalization in the next day.

may be normal or even decreased. Lymphocytosis may reach 80 per cent, with relative neutropenia, there may be, in addition, a percentage of atypical lymphocytes. These changes disappear at the end of the acute stage, when the concentration of eosinophils may increase to high levels.

Blood sedimentation rate is generally moderately elevated Serum turbidity and flocculation tests are generally positive. There is a global hypoproteinemia, with hypoalbuminemia and hyperglobulinemia, caused by an increased value of the alpha$_2$ and gamma globulin fractions, as revealed by paper electrophoresis.

Diagnosis. Fever, generalized edema, lymph node enlargement, hepatomegaly, and splenomegaly in patients from an endemic area should lead to the suspicion of acute Chagas' disease. A detailed history and an accurate physical examination may disclose evidence of the portal of entry of the parasite, i e., the eye's sign (Fig. 8-22A) or the chagoma (Fig. 8-22B). However, these signs are not evident in every case and the diagnosis is difficult when the symptoms are few. Diagnosis may be confirmed with certainty during the acute stage through the demonstration of the parasite by direct blood examination. This may be accomplished by using a drop of flesh blood (thick-drop technique) or by staining a blood smear. The former offers the best results for the detection of the *T cruzi*. This method may give positive results only in the first weeks of infection. The xenodiagnosis test is used chiefly for the diagnosis of chronic Chagas' disease but may show an early positive result during the acute stage (Romaña and Briones, 1954).

Precipitin reaction, using antigen obtained from a *T. cruzi* culture (Muniz and Freitas, 1944), gives positive results in almost every acute case and in about 20 per cent of the chronic forms.

Differential Diagnosis. The inoculation chagoma must be differentiated from similar cutaneous lesions Romaña's sign, or the eye's sign, when not accompanied by the common pattern,



Fig. 8-25 Acute Chagas' disease Roentgenograms taken respectively on the eighteenth (A), twenty-ninth (B), and forty-fifth (C) days after appearance of the signs of infection.

provement ... condition of human dwellings, and ...
agents, ...

Clinical Course and Prognosis The prognosis of acute Chagas' disease is related chiefly to the age of the patient and the character of the manifestations In children, the infection is more severe. The mortality is higher in infants. Dias (1955) reported 29 fatalities (9.7 per cent) in a series of 300 patients with acute Chagas' disease; 17 of the fatalities were in children below 2 years of age. Prognosis is most severe when there is heart failure or meningoencephalitis.

The symptoms of the acute stage may entirely disappear, as may the electrocardiographic and radiologic manifestations (Figs. 8-24 and 8-25). The period of apparent cure without cardiac manifestations may last from 10 to 20 years (Laranja et al, 1956).

Cardiac involvement is slow, but when there is heart failure and arrhythmias or block are present, the prognosis is usually bad. Death is generally sudden and is caused by arrhythmias, AV block, or embolism. Heart failure is frequent as a terminal event

In the authors' series, there were 57 fatalities; 33 (57.9 per cent) were between the ages of 31 and 50 (Fig. 8-34). Sudden death occurred in 40 patients; 13 died from heart failure, and 4 on account of cerebral embolism.

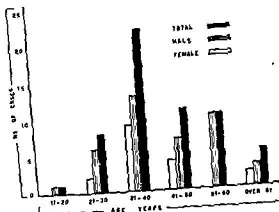
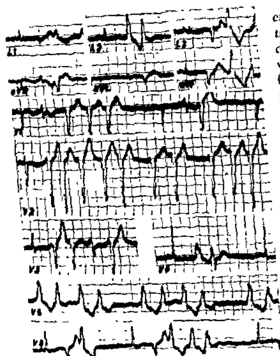


Fig. 8-34. Age distribution at the time of death in 57 cases of chronic Chagas' disease.


Fig 8-33. Chronic Chagas' disease. Runs of multifocal extrasystoles

AMEBIASIS

... abscess adjacent to the pericardial sac in either the liver or the lung.

Carter and Korones (1950) reviewed the literature and found 44 proved cases of suppurative amebic pericarditis. The pericardium becomes thickened, edematous, and infiltrated with inflammatory cells. The parasites may be found in the pericardial fluid. The myocardium is not affected.

Amebiasis is suspected in every patient with amebic abscess of the liver showing signs of pericarditis Final proof is obtained by examining the pericardial fluid obtained by needle puncture This shows a typical "chocolate" appearance.

MALARIA

Malaria is a parasitic febrile disease caused by a protozoon of the genus *Plasmodium* The disease is characterized by episodes of chills, fever, and sweating. These attacks may occur daily (quotidian), every other day (tertian), or with an interval of 3 days between chills (quartan) The tertian form is caused by *P. vivax*, the quartan by *P. malariae*, and the estivoautumnal form by *P. falciparum* The disease is so well known that no detailed description is necessary.

as first shown by Chagas and Villela (1922). A survey carried out in the endemic areas by examining nonselected groups revealed electrocardiographic changes suggestive of Chagas' disease in 15.8 per cent of individuals; in the same community, in a selected group of patients known to have been infected by the *T. cruzi*, 29.2 per cent showed the same electrocardiographic features. Moreover, only 5.7 per cent of persons known to be noninfected showed these electrocardiographic changes. This last percentage is similar to figures obtained from surveys in nonendemic areas (Dias et al, 1953). The incidence is greater in males between 30 and 50 years of age (Fig 8-28).

Signs and Symptoms. Palpitation, precordial pain (different from the pain observed in angina pectoris), and precordial discomfort are the chief complaints. *Dizziness* and *syncope*, sometimes accompanied by an epileptiform attack, occur rather frequently in patients with a slow pulse, paroxysmal tachycardia, or prolonged runs of extrasystoles. Not rarely, patients with severe electrocardiographic and radiologic changes may show only few symptoms or none.

When there is *heart failure*, the symptoms of right side failure are predominant. Isolated left heart failure is rare. The clinical course suggests that right side failure is not secondary to left heart failure; signs or symptoms caused by left heart failure can seldom be elicited. Decreased resistance to exertion gradually develops. *Nocturnal dyspnea* and *orthopnea* are seldom observed. *Hepatomegaly* occurs early and is often accompanied by pain, which may

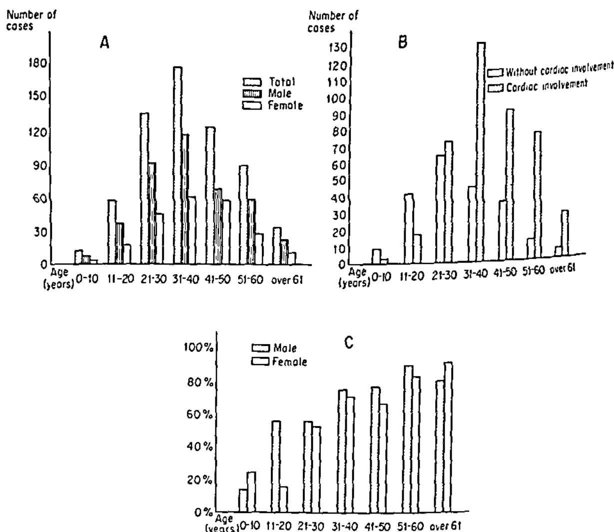


Fig. 8-28. A Sex and age distribution in 642 cases of chronic Chagas' disease. B. Diagram shows greater incidence of chagasic heart lesions in the last decades of life (621 cases) C. Incidence of heart lesions related to sex and age groups (412 cases).

SARCOSPORIDIOSIS

Sarcosporidiosis is caused by certain species of organisms of undetermined nature but described under the generic name of *Sarcocystis*. Among these, *Sarcocystis lindemanni* has been found to cause infection in man. Although several animals, chiefly ruminants and rodents, frequently have the infection, it is rare in man. A probable mechanism of transmission is through contaminated food (Pessôa, 1954). When infection occurs, the sarcocystis invades the skeletal and cardiac musculature. The involved myocardial fiber is usually slightly larger than the adjacent fibers. There is no necrosis or other evidence of reaction to the parasites. No cellular infiltrates are seen (Freitas, 1948) (Fig. 8-35A).

Of the 14 authentic cases on record (Reich, 1954, Freitas, 1948), 7 were found with myocardial involvement. Usually the finding of parasites in the myocardium is incidental in patients dying from various types of disease. There is no treatment for this infection.

HELMINTHIC INFECTIONS

Trichinosis. Trichinosis is an infestation of the striated muscle by the larvae of the roundworm *Trichinella spiralis*. It is transmitted through the ingestion of raw, or inadequately cooked, pork containing live encysted larvae, which are liberated by digestion and anchor themselves to the mucosa of the duodenum and jejunum. After fertilization, the females deposit larvae for a period of approximately 6 weeks and then die. The larvae at first escape into the intestinal lumen, but the majority enter the systemic circulation from the lymphatic vessels and portal system. They follow the blood flow through the right heart and lungs, reaching the systemic arterial circulation between the seventh and twenty-third days (Harrell, 1955).

Larvae are widely distributed to all tissues, including the myocardium, but further development and encystation are possible only in the skeletal muscle (Harrell, 1955). However, invasion of the myocardium causes a picture similar to that of an acute interstitial myocarditis, although it never results in chronic myocarditis (Stryker, 1953). Thrombosis of the femoral artery, resulting in gangrene of the left lower extremity, has been reported (Covey, 1949). This etiologic factor should be considered in cases of thrombosis of a major artery.

Signs and symptoms generally appear after the systemic infestation; they consist of fever, muscular pains, weakness, and edema. The latter may be limited to the upper eyelids or may be diffuse.

Cardiac signs are those commonly seen in myocarditis. Cardiac dilatation, tachycardia, arrhythmias, a systolic murmur, and heart failure may occur in severe cases. Hypotension has been reported as common.

The *electrocardiogram* may show the changes usually seen in acute interstitial myocarditis: low or inverted T waves, small QRS complexes, IV block, grade I AV block. One or more of these changes were present in 21 per cent of 114 cases studied by Solarz (Reich, 1954).

DIAGNOSIS. A clinical diagnosis is seldom made except in typical cases with severe infection. Periorbital edema, tenderness to pressure on the muscles (pain on chewing), and gastrointestinal symptoms are the most useful signs.

Eosinophilia varies from 5 to 70 per cent, and the leucocyte count from 10,000 to 20,000 per mm³. Skeletal muscle biopsy may demon-

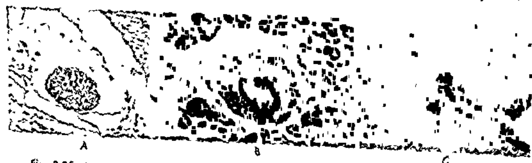


Fig. 8-35. A. Large sarcocystis localized in the specific conduction system of the heart. (Courtesy of Prof. F. Koberle.) B. Schistosoma mansoni worm within a myocardial vessel of the left ventricle. (Courtesy of Prof. W. E. Maffei.) C. S. mansoni eggs surrounded by typical granulomatous lesion in the lung. (Courtesy of Prof. W. E. Maffei.)

TABLE 8-5. ELECTROCARDIOGRAPHIC FINDINGS IN 412 PATIENTS WITH CHRONIC CHAGAS' HEART DISEASE *

Findings	*No. of cases*	*Percentage*
Ventricular extrasystoles	250	60.67
Complete right bundle branch block	178	13.20
Primary T-wave changes	64	15 53
Supraventricular extrasystoles	43	10.43
Complete AV block	38	9 21
Isolated QRS changes	34	8 25
Abnormalities of P wave	30	7.28
Incomplete AV block—first degree	22	5 33
Pattern suggesting anterior infarction	21	5.09
Normal	19	4.61
Atrial flutter or fibrillation	17	4 12
Left ventricular "strain"	16	3 88
Complete left bundle branch block	14	3.39
Incomplete left bundle branch block	12	2.91
Incomplete AV block (2:1, 3:1, 4:1)	9	2.18
Nodal rhythm	5	1.21
	5	1.21
	4	0 96
	3	0 72
	1	0 24
	62	15.04
	10	2 42

* Usually two or more electrocardiographic changes may be seen in the same tracing; the most frequent is the association of ventricular extrasystoles and RBBB.

Multifocal extrasystoles, especially of ventricular origin, are common and usually increase on exertion. Isolated or paroxysmal premature beats are frequently seen. *Atrioventricular block* of various degrees is common Its presence in patients from an endemic area leads to the suspicion of chronic Chagas' heart disease (Fig. 8-30). *Right bundle branch block* (RBBB) is one of the most striking features of the chronic stage Chronic Chagas' myocarditis causes a greater incidence of RBBB in patients from the endemic areas than all the other etiologic factors together. Complete RBBB is associated with a superiorly oriented ÂQRS (Fig. 8-31). The *vectorcardiogram* of these patients revealed different patterns of complete RBBB, with special aspects, such as intraventricular conduction disturbances or loss of electrical forces due to myocardial fibrosis. The vectorcardiogram was found particularly useful in excluding LBBB when routine ECG tracings were misleading (Fehér et al, 1960) (Fig. 8-32).

Primary T-wave changes are observed even in young patients without clinical signs of coronary insufficiency. An electrocardiographic pattern of old anterior infarction, evident in V_3, V_4, V_5, may be found in patients without evidence of coronary heart disease. This was correlated by Carvalhal et al. (1954) with the autopsy findings of degenerative and fibrotic apical lesions.

The variability of the electrocardiographic tracings is one of the most prominent characteristics of the chronic stage of Chagas' disease (Brasil, 1953) (Fig. 8-33). Tracings taken at short intervals (or even one tracing) may display various changes, and finally return to normal or to the previous pattern.

Diagnosis. A history of exposure to the bite of the triatomid insect and findings of arrhythmias lead to the suspicion of chronic Chagas' heart disease. Enlargement of the heart or predominant right heart failure without evidence of valvular lesion is also suggestive of chronic Chagas' myocarditis. A definite diagnosis can be established through the *xenodiagnosis test* or the *Guerreiro-Machado test.*

The xenodiagnosis consists of allowing laboratory-raised, uninfected triatomid insects to suck blood from suspected patients. The material obtained from the hindgut of the insect is then examined for parasites from 30 to 60 days later. This test is the best method for demonstration of the parasite in the chronic stage, but it yields positive results in only 20 per cent of the cases. Therefore, negative results of this test, even in serial examinations, do not rule out the infection.

The complement fixation test, also routinely designated as the Guerreiro-Machado test (1913), is the best method for the diagnosis of chronic Chagas' disease. Several modifications of the original technique have been proposed, but the best results are obtained using the Davis antigen (1943) or the antigen described by Freitas and Almeida (1949). *This test is specific and gives positive results in about 95 per cent of patients with chronic Chagas' disease.*

Differential Diagnosis. Heart symptoms without valvular lesions in young patients who come from an endemic area or have been exposed, even for short periods, to the bite of the triatomid insects point to the diagnosis of

ing. The pulmonary 2d sound is loud and split. Since dyspnea, cyanosis, edema, pulmonary congestion, and enlargement of the liver are frequent, it is difficult to decide whether *or not these signs are caused only by the heart* damage (Barbato, 1952).

Radiologically, there is a gross enlargement of the right chambers and hilar shadows but the peripheral markings are usually clear. Angiocardiography may show a localized vascular enlargement, which corresponds to the pulmonary arteriovenous fistulas (Barbato, 1952).

The electrocardiogram is usually normal in *schistosomiasis* (*Meira and Ramos*, 1944). However, evidence of right ventricular hypertrophy, incomplete RBBB, prolonged P-R interval, atrial fibrillation, LBBB, and tall P waves has been reported (Barbato, 1952).

DIAGNOSIS. The history of having been exposed to the schistosome is important for the diagnosis. However, amebiasis is also common in the regions in which schistosomiasis is endemic. *The finding of schistosoma* ova in the feces contributes to the diagnosis, but failure to demonstrate them is common in certain stages of the disease. Rectal biopsy may demonstrate the presence of eggs. Coutinho (1952) obtained 97 per cent of positive results using the intradermal reaction method, and obtained 96.7 per cent using the complement fixation test.

TREATMENT. Treatment with antimony compounds may be successful. However, *tolerance* to these drugs is low because of their toxicity and the hepatic insufficiency caused by the disease.

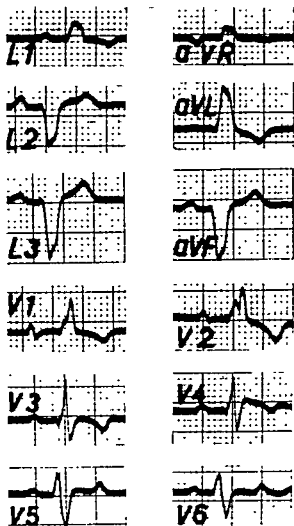


Fig. 8-31. Chronic Chagas' disease; frequently found ECG patterns QRS complex of 0.13 sec, having the pattern of LBBB with superior orientation in the standard leads However, in the precordial leads, it shows a pattern of RBBB

may be associated with Chagas' heart disease should be kept in mind. In such cases, one should not attribute all symptoms and signs to the *T cruzi* infection, even if the diagnosis of Chagas' disease is confirmed by laboratory methods.

Treatment Various chemical agents have been employed They have a variable effect on the parasites in the circulating blood but leave undisturbed the cellular foci of leishmania, rupture of the latter would cause a new invasion of the blood stream In evaluating the results from any treatment of acute Chagas' disease, one should remember that 90 per cent of patients enter a stage of apparent cure, with disappearance of all signs, and that failure to demonstrate *T. cruzi* by laboratory test does not rule out the infection. In the chronic stage, this evaluation is even more difficult because the attempt to demonstrate *T. cruzi* generally fails.

It has been demonstrated that *quinoline derivatives, phenanthridine compounds,* and *sulfurated arsenobenzol* have some trypanocidal action on the circulating forms.

The cardiac symptoms of acute or chronic Chagas' disease can be treated as are symptoms in other types of heart disease, irrespective of the cause. Heart failure in Chagas' disease seems to respond better to diuretics than to digitalis. This is obviously because of the type of myocardial involvement.

Prophylaxis should be directed against the insect vectors through health education, im-

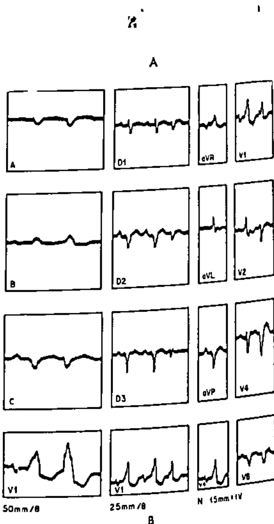


Fig 8-32. A vectorcardiogram of chronic Chagas' disease displaying RBBB with superior orientation of the ÂQRS The QRS loop shows slowing and deformation.

The cardiovascular picture of malaria varies according to the severity of the disease. The benign tertian and quartan forms may show concomitant heart damage as a result of the *anemia* caused by destruction of the erythrocytes. Malignant tertian malaria may show specific lesions caused by *concentration of the parasites within the capillaries of the various organs.* "Microscopic evidence indicates that the coronary occlusions producing anoxemia of the heart may be as important a factor in fatal cases of *P. falciparum* as the occlusions of cerebral vessels" (Merkel, 1946). This may explain the occurrence of *sudden death* of patients in relatively good condition, without heart failure.

Tachycardia, premature beats, syncope, peripheral collapse, and precordial pain have been described as the most common findings. However, there is no agreement on whether malaria is the direct cause of heart failure or of any serious cardiac condition. Sprague (1946) observed in a naval hospital of the United States approximately 2,000 patients with chronic relapsing malaria, in none of them was any cardiac condition discovered that could be specifically attributed to malaria.

Treatment is directed toward eradication of the infection. Chloroquine, pamaquine, and primaquine have been found effective

LEISHMANIASIS

There are various types of leishmaniasis. *visceral leishmaniasis* (*kala-azar*), caused by *Leishmania donovani, cutaneous leishmaniasis* (*oriental sore*), caused by the protozoal parasite *L. tropica, mucocutaneous leishmaniasis* (*American leishmaniasis, espundia, Brazilian leishmaniasis*), caused by a parasite similar to *L. donovani*, which has been called *L. brasiliensis* (Dieuaide, 1955).

Although the parasites show similar appearance, the clinical picture and the geographic distribution are different in each disease. Visceral leishmaniasis (kala-azar) is the only type which may cause myocardial involvement The most heavily infected areas are in Eastern India and Northern China, but the disease is widely distributed in the Sudan, West Africa, Iraq, Southern-Asiatic Russia, and South America.

Kala-azar is characterized by fever, hepato- and splenomegaly, leucopenia, anemia, and hyperglobulinemia. Cardiac manifestations are rare; they may be consequent to myocardial involvement but are not a major feature of the disease. Necropsy findings may show an atrophied heart and, on microscopic examination, myocardial fragmentation and inflammatory cells, including clasmatocytes containing Leishman-Donovan bodies (Stryker, 1953).

The scarcity of information about the cardiac changes in this disease shows that heart symptoms are exceptional, although heart failure may be seen in severe cases. The electrocardiogram may show changes which are not characteristic.

Treatment of the infection with aromatic diamidine compounds (*Neostibosan*) has been successful.

TOXOPLASMOSIS

Toxoplasmosis is caused by microorganisms of the genus *Toxoplasma* which are formed by protoplasmic masses multiplying by binary fission. Dogs, cats, and other domestic animals are the reservoir of this parasite. Parasites have been demonstrated in cow milk, which may be a source of the disease. However, the exact method of transmission in animals and man is not clear yet. The only proved transmission of the disease is congenital. Toxoplasmosis is benign in the mother but may be fatal to the newborn infant (Pessôa, 1954).

Involvement of the myocardium is frequent. However, the central nervous system is the most common site of the infection, and symptoms *are predominantly* related to this location (Stryker, 1953). The parasites are apparently able to invade the fibers of the myocardium without *destroying them or* producing an in- [illegible]

The organisms [illegible] completely filled. The myocardial fibers are completely filled. The *myocarditis* probably results from rupture of parasitized cells which produce an inflammatory reaction in the surrounding tissues. Although the myocardial lesions are not severe, in some cases they may be extensive enough to cause dyspnea and cardiac dilatation.

Very few cases have been studied. Judging by the pathologic findings, it is probable that cases presenting heart failure as the dominant symptom will be recognized (Weinman, 1944).

There is no specific treatment for toxoplasmosis. Experimentally, it has been demonstrated that *sulfonamides* and *Aureomycin* have some action but in doses too elevated for clinical use.

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Pathology of cardiovascular syphilis

BERNARD F. FETTER

Syphilis of the cardiovascular system is not a common disease. In the first 23 years, 7,000 autopsies were performed at Duke Hospital. In this group, there were 148 in which a diagnosis of syphilis of the cardiovascular system was made. The accompanying list indicates the sites which were involved in the 148 cases. Because of the occurrence of the lesions at more than one site, the total is greater than 148. In the case of the aorta, the lesion was classified as aortitis or aneurysm but not both.

Aortitis	107
Aortitis with aneurysm	41
Valves	38
Myocardium	1
Large vessels	9
Coronary	7
Small vessels	2

Disease of the aorta was therefore present in all instances of cardiovascular syphilis. In 28 per cent of these cases the destruction of the aorta had progressed to such an extent that an aneurysm had formed. It may also be noted that 26 per cent of the patients with syphilis of the aorta also developed syphilis of the aortic valve. In the author's series, this was the only valve involved except for one case in which the mitral valve was also affected. In 14 per cent of the cases, the vessels arising from the arch, were affected, chiefly by direct extension of the process.

Syphilis of the cardiovascular system is generally considered a manifestation of the tertiary stage of syphilis. Apparently dissemination of organisms in the body occurs early in the disease but for some, as yet unknown, reason either the organisms become dormant in generalized sites or else they become localized at some site from which dissemination occurs only later. This problem will be further discussed below.

AORTA

Syphilis of the aorta may be seen as either a localized or a diffuse disease, and all gradations of intensity are seen. In Fig. 9-1A, a syphilitic lesion is shown which is localized and about as small as can be seen by the unaided eye. With the aid of the microscope, however, smaller lesions can be seen. At times, the small lesions become confluent, involving the entire aorta (Fig. 9-1B). More commonly the disease process is limited to the thoracic portion. Under such circumstances the aorta may exhibit only scarring, or dilatation may occur. If the *dilatation is uniform*, the circumference of the aorta is increased. Where the disease is *localized*, one may also see *aneurysm* formation either of the *fusiform* or *saccular* type, but most commonly it is saccular (Fig. 9-1C). The development of an aneurysm is, of course, the result of destruction of the wall of the vessel. The most striking changes take place in the elastic tissue of the media, and it was thought for a while that destruction of the elastic tissue was entirely responsible for aneurysm formation. It would seem far more likely that an aneurysm is due to *destruction of all elements of the media*, namely, elastic tissue, muscle, and fibrous connective tissue. The wall of an aneurysm may consist only of collagen, so that in such an instance this element alone is responsible for the strength of the vessel.

strate the presence of the larvae. The most reliable laboratory test is the *serologic reaction* using living trichinella larvae suspended in the patient's serum, which shows a highly refractive precipitate around the worm (Harrell, 1955).

TREATMENT. There is no specific treatment after encystment of the parasite. The administration of ACTH or cortisone may reduce the body reaction to the parasite, decreasing or abolishing the symptoms.

Strongyloidiasis. Strongyloidiasis is caused by *Strongyloides stercoralis.* Although no heart disease is caused by this parasite, rhabitiform larvae have been demonstrated in the pericardial fluid (Froes, 1930) and in the myocardium. The electrocardiogram from the patient with larvae in the myocardium showed only low T waves in leads I and II (Kyle et al., 1948).

Filariasis. Filariasis is an infection caused by one of several filarial worms classified in the family *Filariidae.* Although, in rare instances, the parasite has been demonstrated in the left ventricle, myocardium, or pericardial fluid, the heart failure accompanying filariasis is most probably due to an *allergic reaction* (Giraud et al., 1958; Gerbaux et al., 1956).

Giraud et al. (1958) described heart failure in one patient with filariasis (diagnosed by intradermal reaction with filaria antigen) which subsided with corticotherapy. After disappearance of the clinical signs of heart failure, hemodynamic studies showed modifications similar to those typical of diffuse myocardial or endocardial fibrosis (Robin and Burwell, 1957, Gray, 1951).

Schistosomiasis. Schistosomiasis is caused by one of the three species of schistosomes: (1) *Schistosoma mansoni,* found chiefly in Africa and in the northern part of South America, (2) S *japonicum,* with widespread distribution in the Orient, (3) S *haematobium,* found in Africa, Madagascar, Portugal, and the Middle East.

The infection occurs when the *cercariae,* found in the surface of contaminated water after leaving the host (snails), come in contact with the victim's skin, which they can penetrate, casting off their tails, even if it is unbroken. Although infection may occur through the normal mucosa (buccal), the cercariae cannot survive passage through normal gastric juice. These larvae enter a small vein and, following the blood flow, reach the lungs They are able to pass through the lung capillaries, only those which get into the mesenteric arteries and finally pass through to the portal vessels survive. The remainder are filtered out as foreign protein emboli (Craig and Faust, 1940).

In the portal circulation, the larvae grow and become sexually differentiated, then they migrate against blood flow into the small veins, where they mate, and the fertile females begin laying eggs. Rarely, adult worms may migrate via accessory portal circulation and be carried to the pulmonary arterioles (Craig and Faust, 1940). Generally, the eggs reach the intestinal or vesical lumen and are evacuated with the feces or urine. However, in some cases, the eggs may pass through the hemorrhoidal plexus, penetrating the systemic venous system and thus reaching the lungs (Manzer, 1951).

Lopes de Faria (1956) described the pulmonary changes caused by S. *mansoni,* pointing out the existence of *arteriovenous fistulas* resulting from embolization of small pulmonary arteries by schistosoma ova which cause a necrosis of the arterial wall and that of adjacent veins. These fistulas explain the passage of eggs from the systemic venous system to the arterial venous system. Lopes de Faria (1956) demonstrated S. *mansoni* eggs in the pulmonary veins and in the lumen of a small hepatic artery in a patient with arteriovenous fistulas produced by inflammatory reaction to schistosoma eggs in the lung. These fistulas, besides explaining the passage of the eggs to the systemic circulation, may explain also the cyanosis that is frequently observed in patients with schistosomiasis (Lopes de Faria, 1957).

The presence of eggs or adult worms of S. *mansoni* in the cardiac vessels (Fig. 8-35B) is rarely demonstrated (Barros et al., 1956). The *myocardial reaction* is similar to that seen elsewhere in the organism, especially in the lungs (Fig. 8-35C). Focal inflammatory reaction around the eggs or worms has been described. There is no agreement about the existence of schistosomatic myocarditis; it is denied by the majority of the investigators. On the other hand, the important cardiac changes seen in schistosomiasis are caused by the pulmonary lesions (Barbato, 1952).

As a consequence of the pulmonary changes, there is a ventilatory insufficiency, which explains the frequency of dyspnea. Pulmonary hypertension also may be present, resulting in cor pulmonale. Clinically, a *systolic murmur* at the pulmonary area is the most frequent find-

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cells may be seen about these small vessels in the media of the aorta. The adventitia in these cases is usually greatly scarred and thickened The media is commonly *thinned* (Fig 9-2A) One can frequently *appreciate* these changes with the naked *eye on* examination of the gross *material* The intima of the vessel also shares in the syphilitic process *This structure* commonly undergoes a localized fibrous proliferation The fibrous proliferation plus the scarring produced by the underlying aortitis causes a wrinkling of the surface of the intima usually described *as* resembling *tree bark* There is *longitudinal* wrinkling and also delicate *transverse* wrinkling. Neither of these changes disappears when the aorta is inverted.

The mechanism whereby the above changes are produced is not known Because of the long latent period in the disease, it has been postulated that the changes of necrosis are due to a sensitivity much as one sees in tuber*culosis* This *would* certainly seem entirely plausible in the case of the gumma However, the second lesion described above is clearly not a gumma. It is likely that these changes in the aorta are entirely secondary to changes which have occurred in the vasa vasorum, and *therefore*, the changes in the aorta are those *of incomplete infarction.*

If this is correct, one may then wonder if all cardiovascular syphilis, or more specifically aortitis, is a manifestation of tertiary syphilis. Certainly the gumma would be so considered. The *other variety may, however, be due to an injury which* occurs *much earlier*, possibly at the secondary stage. At this time, the blood *vessels of the aorta* are injured, and as a re*sult of this injury*, the wall of the aorta loses *some of its blood supply. Because of this loss* of blood supply, the muscle fibers die and the elastic tissue and collagen disappear. The latter occurs because *the cells responsible for* maintaining the integrity of these tissues are killed.

From *this point on*, the development of the *aneurysm* would be a simple problem. If the lesion just produced is small, it may heal completely Progression of the process may occur With partial occlusion of circulation through the vasa vasorum, the connective tissue cells of the aventitia proliferate and lay down more

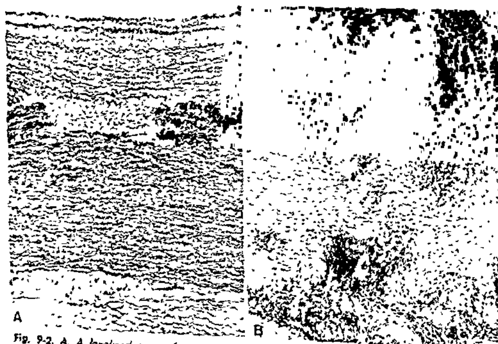


Fig. 9-2. A. A localized area of medial destruction clearly seen in an elastic tissue stain. In the lower portion of the photograph there is scarred adventitia. The wall of the small blood vessel is thickened but this is due to an increase in the muscularis. $\times 106$. *B. Gummatous aortitis. There is a massive infiltration of lymphocytes and plasma cells which is perivascular. The two vessels at the bottom of the photograph show intimal thickening.* $\times 106$.

onstrates a marked narrowing of the coronary orifices. Changes such as these may be the only anatomic lesions recognizable in instances of sudden death Death results apparently from ventricular fibrillation secondary to coronary insufficiency when additional demand is made on an inadequate circulation.

ENDOCARDIUM

Syphilis of the endocardium is almost exclusively a process of extension from adjacent tissue. The most frequently involved area of endocardium is the *aortic valve* Sphyilis attacks this valve chiefly at the commissures (Fig 9-3A) Here, as in the aorta, destruction and healing progress simultaneously. This is attested to by the fact that the leaflets do not rupture in spite of the stress placed upon them while the disease is in progress Scarring at the commissures produces two highly significant effects which act together In the first place the commissures are widened since the valve destruction begins at the point of attachment of the leaflets and healing is accomplished by their adherence to the aorta at points separate from those of original attachment. As a result of *widening of the commissures*, the valve becomes insufficient, the degree of insufficiency varying with the degree of widening. A second process occurs concomitantly with the above further to increase the insufficiency. A characteristic of scar tissue is that it contracts As the healing and scarring take place at the line of attachment of the valve leaflets, the length of the free margin of the leaflets become smaller. As the leaflets become smaller, they are less able to reach the center of the aorta to form a competent valve These two factors then combine to produce an insufficient valve. It readily becomes obvious that *syphilis can never produce stenosis of a valve.*

Microscopically the average case of syphilitic aortic valvulitis is not distinctive The gross appearance enables one to make the diagnosis readily. These gross changes are those described above In Fig. 9-3A the typical changes are shown The first obvious change is a dilatation of the valve ring as a result of aortitis, a fact which contributes to insufficiency of the valve. Secondly, there is a separation of the cusps at the commissures. Thirdly, there is an apparent shortening of the free margins of the valve leaflet. Lastly, there is also a thickening of the leaflets at the commissures which extends onto the free margins.

There is one additional feature commonly seen with aortic valvulitis and insufficiency but not specific for syphilis. This is a transverse ridge of thickened endocardium, usually on the surface of the septum. This ridge may be single, or several parallel ridges may be seen. These are opaque and grayish They measure about 1 cm in length and appear about 2 to 3 cm below the aortic valve ring, always directly beneath a point of incompetence—in this case the widened commissure. This thickening results directly from the regurgitation of blood through the insufficient valve at diastole The jet stream evokes the fibrous proliferation of the endocardium.

The changes described above are the result of an extension of the syphilitic process. Here also, as in the aorta, the changes of the small blood vessels are significant and are responsible for thickening of the valve. The central portion of the valve remains relatively free because it derives most of its nutrition from the large column of blood.

The aortic valve may also be attacked directly by the spirochete, in which case a gumma is produced. Such a lesion was described by Richter in a congenitally deformed valve Should such a lesion occur on a normal valve, it would of course produce a localized area of destruction in the valve leaflet. Such a leaflet would either rupture as a result of the necrosis of tissue or become greatly thickened as a result of healing In either case, the lesion would not appear as the characteristic syphilitic valvulitis but would instead appear as a fibrosis or destruction of a single leaflet, with the other two leaflets appearing normal.

MYOCARDIUM

Syphilis of the myocardium may also occur. The incidence, as in many other diseases, depends upon who is reporting the cases and what his criteria are Gore and Saphir, in studying 1,400 cases of myocarditis, reported two cases of syphilitic myocarditis Both of them were classified as gummatous. The author has had the opportunity to see a similar case. In this instance there was a gumma in the left ventricle. The gumma may occur anywhere,

Destruction of the wall of the aorta is a slow process which allows healing and destruction to occur concomitantly. It is for this reason that aneurysms may grow to large sizes before they rupture. When a rupture takes place, this means that the destructive changes in the aorta have progressed more rapidly than the healing. Rupture may occur into any of the adjacent structures. Hemorrhage is usually massive and fatal One of the most interesting cases the author has had the opportunity to study was a 58-year-old man in whom an aneurysm of the ascending aorta ruptured into the superior vena cava. This occurred 5 days prior to death. Death was attributed to congestive failure

An aneurysm, in addition to the fact that it may rupture, becomes significant also from its presence as *a pulsating mass* It may attain sufficient size to cause a profound decrease in respiratory function. By stretching the left recurrent laryngeal nerve, an aneurysm of the arch will produce *paralysis of the left vocal cord* The author has seen an aneurysm of the descending aorta which destroyed almost half of the center of the thoracic vertrebrae The intervetebral disks, being elastic, were able to withstand the continuous trauma The ribs and sternum may likewise be eroded

Microscopically, syphilis of the aorta appears in two forms. The first of these is the *gumma* (Fig. 9-2B), so-called because of its rubbery consistency. This lesion is the same as the gumma seen elsewhere and is characterized by a coagulative necrosis of exudate and fixed tissues, with a large number of round cells comprising the cellular exudate The consistency of the lesion is due to the proliferation of fibroblasts with the deposition of collagen. The round cells which appear in the cellular exudate are lymphocytes, plasma cells, and reticuloendothelial cells. The latter, because of their great reactive potential, appear in several forms. They may be seen as macrophages, epithelioid cells, or even as multinucleated giant cells of the Langerhans variety. At times, the microscopic lesion bears a striking resemblance to the tubercle of tuberculosis. At such times, it is necessary to demonstrate the spirochete by specific staining techniques before a definitive diagnosis can be made.

The second and more common form in which syphilitic aortitis is seen is one manifested by a *perivascular infiltration* of lymphocytes and plasma cells This perivascular infiltration is most prominent about the vasa vasorum in the adventitia, although the same



Fig. 9-1. A. A small localized lesion in the terminal portion of the arch of the aorta. From the gross appearance, it cannot be determined whether this lesion is healed or will progress. (*From Forbus Reaction to Injury, Williams & Wilkins, 1943*) B. A more extensive aortitis showing the characteristic wrinkling. Note also the narrowing of the ostiums of the intercostal arteries. Compare this photograph with (A). C. A massive saccular aneurysm of arch of aorta. The dark area represents laminated thrombus Characteristic changes of aortitis may also be seen in the remainder of the aorta.

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There is one additional feature commonly seen with aortic valvulitis and insufficiency but not specific for syphilis. This is a transverse ridge of thickened endocardium, usually on the surface of the septum. This ridge may be single, or several parallel ridges may be seen These are opaque and grayish. They measure about 1 cm in length and appear about 2 to 3 cm below the aortic valve ring, always directly beneath a point of incompetence—in this case the widened commissure. This thickening results directly from the regurgitation of blood through the insufficient valve at diastole The jet stream evokes the fibrous proliferation of the endocardium.

The changes described above are the result of an extension of the syphilitic process. Here also, as in the aorta, the changes of the small blood vessels are significant and are responsible for thickening of the valve. The central portion of the valve remains relatively free because it derives most of its nutrition from the large column of blood.

The aortic valve may also be attacked directly by the spirochete, in which case a gumma is produced Such a lesion was described by Richter in a congenitally deformed valve Should such a lesion occur on a normal valve, it would of course produce a localized area of destruction in the valve leaflet Such a leaflet would either rupture as a result of the necrosis of tissue or become greatly thickened as a result of healing In either case, the lesion would not appear as the characteristic syphilitic valvulitis but would instead appear as a fibrosis or destruction of a single leaflet, with the other two leaflets appearing normal

MYOCARDIUM

Syphilis of the myocardium may also occur. The incidence, as in many other diseases, depends upon who is reporting the cases and what his criteria are. Gore and Saphir, in studying 1,400 cases of myocarditis, reported two cases of syphilitic myocarditis Both of them were classified as gummatous. The author has had the opportunity to see a similar case In this instance there was a gumma in the left ventricle. The gummi may occur anywhere,

Destruction of the wall of the aorta is a slow process which allows healing and destruction to occur concomitantly. It is for this reason that aneurysms may grow to large sizes before they rupture. When a rupture takes place, this means that the destructive changes in the aorta have progressed more rapidly than the healing Rupture may occur into any of the adjacent structures. Hemorrhage is usually massive and fatal One of the most interesting cases the author has had the opportunity to study was a 58-year-old man in whom an aneurysm of the ascending aorta ruptured into the superior vena cava. This occurred 5 days prior to death. Death was attributed to congestive failure.

An aneurysm, in addition to the fact that it may rupture, becomes significant also from its presence as *a pulsating mass* It may attain sufficient size to cause a profound decrease in respiratory function. By stretching the left recurrent laryngeal nerve, an aneurysm of the arch will produce *paralysis of the left vocal cord* The author has seen an aneurysm of the descending aorta which destroyed almost half of the center of the thoracic vertrebrae The intervetebral disks, being elastic, were able to withstand the continuous trauma. The ribs and sternum may likewise be eroded.

Microscopically, syphilis of the aorta appears in two forms. The first of these is the *gumma* (Fig. 9-2B), so-called because of its rubbery consistency. This lesion is the same as the gumma seen elsewhere and is characterized by a coagulative necrosis of exudate and fixed tissues, with a large number of round cells comprising the cellular exudate. The consistency of the lesion is due to the proliferation of fibroblasts with the deposition of collagen The round cells which appear in the cellular exudate are lymphocytes, plasma cells, and reticuloendothelial cells. The latter, because of their great reactive potential, appear in several forms They may be seen as macrophages, epithelioid cells, or even as multinucleated giant cells of the Langerhans variety. At times, the microscopic lesion bears a striking resemblance to the tubercle of tuberculosis. At such times, it is necessary to demonstrate the spirochete by specific staining techniques before a definitive diagnosis can be made.

The second and more common form in which syphilitic aortitis is seen is one manifested by a *perivascular infiltration* of lymphocytes and plasma cells This perivascular infiltration is most prominent about the vasa vasorum in the adventitia, although the same



Fig. 9-1. A A small localized lesion in the terminal portion of the arch of the aorta From the gross appearance, it cannot be determined whether this lesion is healed or will progress. (From Forbus Reaction to Injury, Williams & Wilkins, 1943) B. A more extensive aortitis showing the characteristic wrinkling. Note also the narrowing of the ostiums of the intercostal arteries. Compare this photograph with (A) C. A massive saccular aneurysm of arch of aorta. The dark area represents laminated thrombus. Characteristic changes of aortitis may also be seen in the remainder of the aorta.

2

Clinical aspects of syphilis and syphilitic heart disease

JACOB S. GOLDEN

The relative importance of syphilis in relation to cardiovascular disease in the United States has been profoundly and significantly altered during the past two decades Two major factors have been responsible for the conclusive demonstration that syphilis is a preventable cause of heart disease The passage of the *National Venereal Disease Control Act* in 1938 marked the beginning of the present venereal disease program Today, although syphilis is still present, the incidence of primary infections is considerably reduced Aggressive public health measures for the detection and treatment of latent syphilis have resulted in a marked reduction of the incidence of late cardiovascular syphilitic lesions The *second major factor has been the therapeutic* employment, since 1943, of *penicillin*, which has proved to be a highly effective spirochetocidal and curative agent

Accurate knowledge of the prevalence of syphilis in the United States was not available prior to 1941 Except during and immediately following war years, the incidence of fresh infections in the United States and Western Europe has declined over the past 100 years In the United States, the decline was particularly precipitous from the peak incidence of 107,000 cases in 1947 to only 12,000 in 1952 During the period 1953 to 1955, the annual incidence continued to diminish but the rate of decline tended to level off During 1956, the number of fresh cases actually increased by 7 1 per cent Sustained intensification of venereal-disease control is required to halt this reversal of a 10-year downward trend.

From 1933 to 1939, the average yearly death rate from syphilis was between 15 and 16 per 100,000 population Disability and mortality due to syphilis have steadily decreased in the United States since 1940 when the death rate per 100,000 population was 10 7 By 1951, the rate had declined to an estimated 4 7, representing about 7,000 deaths, a reduction of over 50 per cent

Welty, from a survey of necropsy material over a 10-year period from 1927 to 1937, found a definitely decreasing incidence of cardiovascular syphilis in all forms and as a cause of death He explained the decrease as due to "modern methods of therapy" Prior to 15 years ago, the necropsy incidence of cardiovascular syphilis was approximately 10 per cent of all cardiac diseases. The present necropsy incidence is probably less than one-half of 1 per cent of diseased hearts in sections of the United States where the population is predominantly white In 1953, White, reporting on the morbidity and mortality from cardiovascular syphilis in New England, noted a decrease from 3 9 per cent of cases of heart disease to 1 per cent He remarked on the rarity with which a syphilitic aneurysm is seen at the Massachusetts General Hospital and predicted that "in another generation cardiovascular syphilis should be, in New England, simply a historic disease of the past, as it can become in any part of the world."

In 1953, Bauer noted that, although there had been a consistent decrease in the number of cases of infectious syphilis, there was still a "reservoir estimated at 2,100,000 persons with latent and late syphilis in the population who must be sought out and brought to treatment" Although it is difficult to estimate the results of lack of treatment in this group, there is evidence that about 8 to 10 per cent, representing about 170,000 cases, will

collagen. This proliferation serves as a splint to the now defective aorta If the sclerosis of the vasa increases, the new tissue also dies. The formation of an aneurysm is a delicate balance between the destruction of old tissue and the formation of new In large aneurysms, the wall of the sac is formed entirely of scarred adventitia.

An alternate explanation would be that the latter lesion, described above as related to the vasa vasorum, may have another origin. It may be that the spirochete has directly injured the wall of the aorta and caused destruction of tissue Such destruction would evoke a *mononuclear response* which would persist long after the spirochetes were no longer demonstrable. Indication of destruction having occurred is found in the perivascular cellular infiltrate. The changes in the vasa vasorum which are described above as a primary cause of destruction would, under this line of reasoning, be considered as resulting from a decreased need for the blood supply. These vessels would then undergo obliterative changes in the intima characterized by an intimal proliferation This proliferation is known by the rather inappropriate name of "endarteritis obliterans" It is commonly seen in vessels supplying tissues in which destruction has taken place, for example in the larger arteries of the kidney in cases of hypertension.

The author does not claim to know which of the above explanations is correct. Certainly one would have adequate justification to support either view. As far as the idea of direct injury to the aorta is concerned, one tends to consider such areas as localized This is not necessarily correct. Certainly tiny localized areas of destruction may coalesce as do the tubercles in tuberculosis. The lesions may begin to heal at any time in their development so that one would certainly expect a wide variety of microscopic changes, which, in fact, one does see.

An additional change which takes place in aortitis is intimal alteration. This takes the form of a fibrous proliferation which is not unlike the changes of arteriosclerosis In fact, *arteriosclerosis may be superimposed upon the syphilitic process,* so that interpretation at an advanced stage of the combined process may become impossible. As one would suspect, intimal proliferation is significant only at the ostia of the vessels arising from the aorta. *The ostia become narrowed by the process and may become completely occluded.* Figure 9-3 dem-



Fig. 9-3. A Aortitis with extension to valve Syphilis of the first portion of the aorta has extended into the valves. The commissures are widened, and the leaflets are scarred at this point. The small spot in the center of the photograph represents one of the coronary orifices greatly narrowed by the proliferative reaction. (*Reprinted from Forbus Reaction to Injury, William & Wilkins,* 1943.) B. Aortitis localized to the same region as in (A), except that there is no extension into the valves. The coronary orifice is narrowed but not to the same degree as in (A). The circumference of the aorta is increased.

complicating nonaneurysmal aortic dilatation, coronary ostia stenosis, or associated nonsyphilitic cardiovascular disease. The designation "uncomplicated syphilitic aortitis" is more correctly assigned to an incidental autopsy finding which has no clinical counterpart. Necropsy statistics indicate that syphilitic aortitis is present in 80 to 90 per cent of patients with syphilis who had been untreated or inadequately treated during the early stages. *From a practical clinical viewpoint, therefore, it may be assumed that all persons with latent syphilis, untreated or inadequately treated, have syphilitic aortitis.* The diagnosis of uncomplicated aortitis is made by inference

NONANEURYSMAL AORTIC DILATATION

Moore et al., from a study of 105 cases of syphilitic aortitis proved by autopsy, recommended criteria for the diagnosis of "uncomplicated syphilitic aortitis." The criteria included symptoms and physical and roentgen findings Subsequent clinical investigators questioned the validity of the criteria as evidence of the uncomplicated phase and considered them as manifestations of advanced syphilitic aortitis or of other forms of cardiovascular disease, especially hypertension, rheumatic and calcific aortic valvulitis, and atherosclerosis of the aorta and coronary arteries. *Nonaneurysmal dilatation of the ascending aorta or the arch in the absence of hypertension or rheumatic valvular disease in patients under 40 years of age is highly suspicious of the presence of syphilitic aortitis*

Symptoms. There are no symptoms attributable to simple aortic dilatation per se Precordial pain, in syphilitic patients under 40 years of age, is due to associated coronary ostia stenosis In older patients, coronary arteriosclerosis may be responsible *Paroxysmal nocturnal dyspnea* and symptoms and signs of heart failure likewise arise from associated coronary ostial narrowing, aortic insufficiency, or other cardiovascular abnormalities comprising the blood supply of the myocardium Keefer and Resnik observed no instance of paroxysmal nocturnal dyspnea in 24 necropsied cases in whom no other responsible lesions were present

Physical Signs. The presence of nonaneurysmal aortic dilatation is suggested by the detection of one or more of four abnormal physical findings These are an *altered quality and intensity of the 2d aortic sound, a systolic murmur at the aortic area, increased supracardiac dullness,* and *abnormal anterior thoracic pulsations.* None are pathognomonic of syphilitic aortic dilatation. Their clinical significance requires correlation with the patient's age and clinical history and with other existing abnormalities. An accentuated *low-pitched tambour 2d aortic sound* has been described as characteristic of syphilitic aortitis with or without dilatation It is of particular diagnostic value when associated with other evidence of aortic dilatation in younger patients with a history of syphilis or with positive serologic reactions Boharas et al. found a *tympanitic 2d aortic sound* in 5 of 200 syphilitics under 50 years of age and only once in 800 nonsyphilitics of the same age group They considered this physical sign to be of diagnostic value for the detection of syphilitic aortitis when other causes are first excluded Dilatation of the aorta due to hypertension or aortic atherosclerosis may be associated with an accentuated 2d aortic sound which is more often bell-like or ringing in quality In 61 patients with syphilitic aortitis not complicated by aortic insufficiency or aneurysm and whose average age was over 50, Irvine found the 2d aortic sound accentuated in 23.

Dilatation of the ascending aorta immediately distal to the aortic ring, causing a functional aortic stenosis, may be accompanied by a *systolic murmur* It was detected in 78 of 141 cases of syphilitic aortic dilatation diagnosed clinically (Rich and Webster). The murmur is best heard in the 2d right intercostal space near the sternum and is usually less harsh than the murmur associated with organic stenosis of the aortic valve or with aneurysm of the root of the aorta. Since aortic dilatation may be associated with other etiologic factors such as atherosclerosis of the aorta, hypertension, or rheumatic aortic insufficiency, the diagnostic significance of the murmur is greater in patients under 40 years of age and who are free of disease other than syphilis.

In the absence of appreciable emphysema, *increased supracardiac dullness* is elicited in the presence of moderate dilatation of the ascending aorta and of the arch With dilatation of the ascending aorta, right upper parasternal

however. The lesions in the heart muscle may heal, or they may extend to produce endocarditis or pericarditis.

Syphilis of the myocardium has been said to occur in a second form. The advocates of this idea say that the heart muscle is diffusely infiltrated by fibrous tissue, with occasional small round cells. The diagnosis in such a case is made on the basis of the fact that the scarring is seen in an individual whose coronary vessels do not show gross alterations and that no other logical explanation is available. There is no reason to believe that the heart is immune to the spirochetal action except in so far as a gumma may be produced. To state categorically that cases of diffuse myocardial fibrosis without obvious explanation are due to syphilis, even in the presence of a positive serologic test for syphilis, is indefensible.

CORONARY ARTERIES

Extension of the syphilitic process in the aorta becomes significant in still another instance Syphilis has a predilection for the first portion of the aorta, and it is here that the coronary vessels arise. The destructive lesion of syphilis sometimes extends into the sinus of Valsalva. When it does, it surrounds the coronary ostia (Fig 9-3) In the subsequent healing, there is a proliferation of the fibrous tissue of the intima in such a way that a cushion of fibrous tissue develops about the ostium, producing a partial occlusion. This lesion will behave exactly as does coronary arteriosclerosis It may be the only lesion seen in the heart in cases of sudden death The supposition in such cases is that the ostium has been sufficiently narrowed so that the heart is functioning with a coronary circulation of borderline efficiency Any sudden demand on the circulation results in a coronary insufficiency which produces ventricular fibrillations

Syphilis of the coronary vessels is not entirely a disease of the ostia Moutz (1931) studied this problem specifically. In eight cases of coronary artery disease in syphilitic patients, all had significant narrowing of the ostia In six of the cases, there was, in addition, intimal proliferation and fibrosis in the first portion of the vessels which, at times, had the appearance of well-vascularized granulation tissue. *Changes within the coronary vessels may lead to infarction.*

PULMONARY ARTERIES

Syphilis may also involve the lesser circulation, but this is unusual. There may be produced a *pulmonary arteritis* and, as a result of extension of the process, even a *pulmonary valvular insufficiency.*

PERIPHERAL BLOOD VESSELS

Syphilis of the peripheral blood vessels is not a significant disease. The major branches of the aorta have been mentioned above. Of these, the most significant are the coronary arteries, which may have their ostia narrowed by syphilis in the aorta or which may be the seat of syphilitic infection directly. As stated above, where syphilitic coronary arteritis exists, it is usually confined to the first centimeter of the vessel. Similar changes may also be seen about the other branches from the aorta.

The smaller blood vessels are also affected by syphilis. In the discussion of syphilitic aortitis, the role of syphilis of the vasa vasorum is noted. If one considers this involvement as primary, then one must conclude that syphilis of the small blood vessels is highly significant. Certainly one must say that the smaller vessels are affected in the secondary phase of syphilis. The production of the rash depends upon the dilatation of existing vessels or upon the formation of new ones. Whether this is a primary lesion of the vessels or whether the vessel lesion is secondary to changes in the tissues cannot be stated.

clavian arteries are less frequently affected Rarely, *stenosis of* the mouths of the renal arteries leads to renal ischemia and hypertension (Saphir).

Stenosis of the Coronary Ostia. Stenosis or occlusion of one or both coronary ostia is present at *necropsy in* 10 to 35 per cent of *patients* with cardiovascular syphilis. More frequently, both ostia are stenosed

In patients with coronary ostia involvement as the only complication of syphilitic aortitis, symptoms may not appear *even* though stenosis of both ostia is of severe degree At this stage, the ECG usually reveals *no* evidence of *myocardial ischemia* *When* compensatory collateral circulation fails to keep pace with the rapidity of orifice narrowing, myocardial nourishment and function become impaired and symptoms ensue Since, in most instances, it *is common* for aortic insufficiency to coexist and because hypertension and coronary sclerosis are frequently concomitant after the fourth decade, clinical manifestations may not be readily distinguished.

Precordial pain and *heart failure* are the significant clinical consequences The pain is of the same character as that caused by advanced coronary *sclerosis but is often more severe* and *responds* less favorably to nitroglycerin *Severe protracted pain* and *sudden death* before the clinical picture of acute myocardial infarction has *time to* unfold, are not infrequent As already noted, myocardial *infarction is an* uncommon necropsy finding in patients with cardiovascular syphilis The pain of an associated aneurysm of the *ascending* aorta is characteristically more constant, *does not tend to* radiate, and results from *pressure on neighboring* mediastinal structures Precordial pain in a *young* syphilitic man should point to coronary ostia narrowing as the cause

Following the onset of exertional dyspnea and other clinical signs of *incompetent myocardial* function, the course is one of rapid and *progressive* deterioration. In the absence of aortic insufficiency or hypertension, the heart may be *of normal* size or moderately enlarged. Atrial fibrillation is *uncommon. The response* to therapeutic measures for congestive heart *failure is* unfavorable Digitalis is ineffective. Episodes of *paroxysmal nocturnal dyspnea* or *acute pulmonary edema* in patients with coronary ostia stenosis may occur, but in such instances, accompanying aortic insufficiency or hypertension is probably the *most significant* causative factor.

In summary, stenosis or occlusion of the orifices of the coronary *arteries* is clinically suspect when, in a syphilitic patient under 40 years of age, precordial pain or heart failure (*which is rapidly* progressive and responds poorly to therapy) occurs.

Stenosis of the Ostia of Other Branches of the Aorta. Inequality of blood pressure and arterial pulsations in the upper extremities (*pulsus differens*) or diminished pulsation *of* either carotid artery in patients with syphilitic aortitis may be indicative of stenosis of the orifices *of one or more branches of the aortic* arch. Syphilitic aortitis, with or without aneurysm, is the most common cause of the so-called "aortic arch syndrome." Even in the presence of aneurysm, the stenosis is usually due to intimal thickening rather than to thrombotic occlusion Rarely are all three major ostia stenosed In such cases, the arterial pulsations in the upper part of the body *are diminished* while hypertension is present in the lower extremities Reflex vasoconstriction *secondary to* ischemia of the vasomotor center, or to stimuli from receptors of the carotid arteries, is suggested as a possible mechanism for the hypertension in the lower extremities. *Dizziness* and *fainting* are prominent symptoms

SYPHILITIC AORTIC INSUFFICIENCY

Aortic insufficiency is the most frequent complication of syphilitic aortitis. When considered in relation to the incidence of syphilis, it is not common, occurring in 3 to 4 per cent of cases In necropsied *patients* with advanced cardiovascular *syphilis*, deformity of the aortic ring *and of the cusps is present in 20 to* 35 per cent. The clinical incidence of aortic insufficiency *is* reported in as high as 50 to 60 per cent of *patients* with cardiovascular syphilis. The incidence in men is much greater than in women, the ratio *ranging as high* as *10:1* The racial frequency *depends* upon the population studied. *Syphilitic* aortic insufficiency is more common *among* Negroes, in whom *it is diagnosed* at a younger age The majority of white patients *with this* complication are between 35 and 50 years of age.

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insufficiency. Finally, in advanced cases, a *rumbling mid-diastolic murmur* may be heard just within the apex. This is *known as the Austin Flint murmur*. It is due to "relative mitral valve stenosis" and occurs when *aortic* valve incompetency is primarily of the posterior cusp. This phenomenon may be *difficult* to differentiate *from an acquired* mitral stenosis in a patient with aortic insufficiency and positive serologic reactions for syphilis. The Austin Flint murmur, however, is *not characteristically* accompanied by an accentuated 1st apical sound or opening snap of the mitral valve; a *presystolic thrill is infrequent*, the murmur is less intense, and the associated physical signs of acquired mitral stenosis are lacking. At times, differentiation is *not possible*.

The heart itself may be of normal size if the degree of aortic valvular incompetence is *minimal*. With appreciable regurgitation, the left ventricle enlarges so that the apex may be seen in the 6th and 7th intercostal space as far to the left as the *anterior* axillary line. As already noted, most of the heaviest hearts recorded *result from* hypertrophy of the left ventricle secondary to syphilitic aortic insufficiency. Typically, the pulmonary artery–conus region is not enlarged on percussion to the left of the midparasternal region. Percussion of the upper sternal and parasternal regions may reveal the presence of aortic dilatation or aneurysm. The peripheral arterial phenomena associated with an appreciable aortic leak are usually readily detectable and include the *water-hammer type of pulse, high systolic and low diastolic blood pressures, pistol-shot sounds over the femoral arteries*, Duroziez' sign, and *capillary pulsation*. The systolic arterial pressure differential, normally higher in the lower extremities, is increased. With lesser grades of aortic insufficiency, the peripheral signs *may* be minimal or absent. This is also the case when diastolic hypertension coexists.

The clinical course of syphilitic aortic insufficiency *may be modified* by retroversion or eversion or by rupture of an aortic cusp. *Retroversion* occurs when a thickened and sagging cusp, most *frequently the anterior*, has been deprived *of its* supporting elastic framework. With *either retroversion or sudden rupture*, there is chest pain, shock of moderate *degree*, and acute left heart failure, which *may* be rapidly fatal. Some patients, however, have survived for several *months*. The distinguishing physical finding is the appearance of a *loud musical diastolic murmur* audible over the entire precordium, but most intense at the base and often widely transmitted to the posterior thorax, head, and upper extremities. It may be so pronounced as to be troublesome to the patient and as to be heard at a distance from the anterior thoracic wall. Many descriptive qualities have been used to describe the *murmur*: these include "croaking of a frog," "cooing of a dove," "humming," "buzzing," "whistling," etc. A diastolic thrill over the base may be detected.

Roentgen Examination. As the left ventricle progressively enlarges, the apex becomes *rounded*, and the silhouette extends outward and downward toward the left lateral chest wall. The aorta may be of normal or increased width. Aneurysmal dilatation may be present. In Moore's series, the width of the aorta was normal in 43 per cent of the patients with syphilitic aortic insufficiency. On fluoroscopic examination, the heart pulsations, as well as that of the aorta, are increased. A "dancing" aorta is noted with free regurgitation.

Electrocardiography. The changes from the normal, when present, are those of progressive *left ventricular hypertrophy or strain*. Arrhythmias, other than premature contractions, are not common. Atrial fibrillation is usually absent, even when congestive failure exists. Evidence of myocardial infarction is infrequent even when severe coronary ostia stenosis is associated with syphilitic aortic insufficiency.

Differential Diagnosis. The clinical problems involved in the differential diagnosis of aortic insufficiency have been modified during the past decade. Previously, advanced syphilitic cardiovascular lesions occurred most frequently in the fourth and fifth decades, and the incidence in patients beyond 60 years of age was between 15 and 35 per cent. The decreasing incidence of syphilis, a more aggressive public health program for the detection and treatment of latent syphilis, and the greater effectiveness of modern therapy are responsible for the fact that cardiovascular syphilis is increasingly becoming a disease of older persons. As a result, clinicians must be aware that the classical features of syphilitic lesions are modified in this group by the more frequent combination with aortic and coronary arteriosclerosis and hyper-

develop late cardiovascular manifestations Physicians should, therefore, expect diagnostic and therapeutic problems involving late syphilis of the heart and aorta for at least a generation. It is necessary to search diligently for cases of latent and late syphilis in order to reduce the size of the reservoir in the general population.

DIAGNOSIS OF SYPHILIS

Confirmation of a clinical impression that syphilis is the cause of cardiovascular disease in an individual patient is obtainable from the medical history and from the physical and laboratory examinations. The history of a *primary genital lesion* or of *past diagnosis and specific treatment* is diagnostic. However, knowledge or recall of a primary lesion, especially in female patients, may be lacking or faulty. A history of *multiple miscarriages* and *stillbirths* constitutes presumptive evidence Physical examination may reveal, in addition to a genital scar, other syphilitic stigmas involving the skin or the osseous and central nervous systems. Approximately one-third of patients with cardiovascular syphilis have signs of *central nervous system involvement Syphilitic aortitis* and its complications occur in an appreciable number of patients with neurosyphilis Evidence obtained from neurologic examination can, therefore, aid in establishing the presence of syphilis as the etiologic agent of cardiovascular disease. Of particular significance, neurologically, are pupillary abnormalities, palsies, and diminished or absent deep tendon reflexes. *Examination of the cerebrospinal fluid* may reveal abnormalities of the cellular elements and protein content, as well as positive specific serologic and gold-curve changes.

In the past, 15 per cent of patients with cardiovascular syphilis have had negative (blood) standard serologic tests With recent techniques, serologic reactions are positive in over 95 per cent. In 1949, Nelson and Mayer introduced the *treponemal immobilizing antibody test.* This test is helpful in establishing the presence of syphilis in patients with late manifestations in whom the standard tests are negative and other stigmas of syphilis are not apparent

PREDISPOSING ETIOLOGIC FACTORS OF CARDIOVASCULAR SYPHILIS

The clinical manifestations of cardiovascular syphilis appear with increasing frequency through the fourth and fifth decades. It is uncommon for symptoms to appear before the age of 35. Late syphilitic lesions, however, have been reported in persons under 20 years of age. Such lesions are rarely the result of congenital syphilis. McCulloch, from a study of 40,470 children among whom 939 had congenital syphilis, found no evidence of cardiovascular syphilitic lesions. Congenital syphilis does not contribute to the incidence of heart disease up to the age of 15.

The incidence of syphilitic heart disease is predominantly higher in *males.* Reported ratios vary between 2:1 and 5:1. Primary syphilis occurs more frequently in men. The effect of *physical exertion* upon intraaortic pressure may be responsible for the much higher incidence of aortic dilatation and aneurysm.

The statistical incidence of syphilis and syphilitic heart disease varies with the population studied by various investigators. Social and economic status are important factors It is, therefore, not remarkable that the frequency of late cardiovascular syphilitic lesions is greater among Negroes. In the latter race the symptomatic phase of syphilitic aortitis and its complications commence earlier and the course of the disease is shorter.

UNCOMPLICATED OR SIMPLE SYPHILITIC AORTITIS

Despite the lack of specific treatment for early syphilis, between 60 and 70 per cent of patients go through life without clinical manifestations of tertiary lesions Approximately 10 per cent develop advanced cardiovascular lesions Between the onset of the specific inflammatory process in the aorta during the early months of the infection and the appearance of clinical evidence of syphilitic heart disease, there is a latent period of 10 to 20 years or more During the latent phase, progressive pathologic changes occur with varying tempo, depending upon the patient's race, sex, occupation, and the adequacy of delayed specific therapy. Of prime importance in preventing or retarding the development of late cardiovascular complications is the clinical detection of patients with uncomplicated or simple syphilitic aortitis Some clinical investigators have recommended criteria for the diagnosis of uncomplicated aortitis. These criteria, however, are indicative of the existence of

if ever, is superimposed on an aortic valve deformed by syphilis alone. The syphilitic pathologic alterations of the leaflets, unlike those of rheumatic valvulitis, do not favor bacterial surface infection. When the latter occurs, *a third factor, usually rheumatic valvulitis, is present.* In the five cases of associated cardiovascular syphilis and bacterial endocarditis cited by Koletsky, stigmas of rheumatic heart disease were demonstrated unequivocally in four, and there was combined syphilitic and rheumatic aortic valvular disease in at least two. The rheumatic valvular lesion may be slight or obscured and easily overlooked.

Prognosis. In general, the long-term prognosis of syphilitic aortic insufficiency is good. In about 50 per cent of the patients, there is an asymptomatic period varying from 2 to 10 years after the lesion is detected. Moore et al., from a study of 1,020 cases, found that 33 to 43 per cent lived 10 years and 20 to 30 per cent survived for 15 years from the time of diagnosis. In women, the course is more favorable. A more rapid downhill course in Negroes is favored by an accelerated tempo of the disease, less favorable economic conditions, and inadequate specific therapy before and after the diagnosis. Following the onset of symptoms, the average survival period is usually 3 to 4 years. However (especially when antisyphilitic therapy is instituted), many maintain compensation, are capable of working, and live 10 to 14 years. Once heart failure develops, the prognosis becomes unfavorable. Only 6 per cent of Moore's series with heart failure at the time of diagnosis survived 10 years. Precordial pain is definitely an unfavorable prognostic symptom.

AORTIC ANEURYSM

Etiology. Aneurysms of the aorta are, with few exceptions, the result of either syphilis or arteriosclerosis. Syphilis has been responsible for 95 per cent of aneurysms of the thoracic aorta. Arteriosclerosis is the cause of a large majority of aneurysms of the abdominal aorta below the origin of the renal arteries. The relative incidence of syphilitic and arteriosclerotic aneurysms in any section of the population corresponds roughly with the prevalence of venereal disease. During the past two decades, there has been a marked decrease in the incidence of syphilitic aneurysms. Cranley reviewed 17,168 autopsies performed at the Cincinnati General Hospital from 1926 to 1952 and reported a decrease of syphilitic aneurysms from 1 in 46 autopsies between 1926 and 1930 to 1 in 696 from 1951 to 1952. Increased longevity, however, has resulted in both a relative and an absolute increase in the occurrence of arteriosclerotic aneurysms of the abdominal aorta.

Whereas the ratio of syphilitic to arteriosclerotic aneurysms of the abdominal aorta was formerly 8:1, the ratio in recent years has been less than 3:1. Wright reviewed 107 cases of abdominal aneurysm observed at New York Hospital between 1945 and 1955 and found just one instance in which syphilis might have been the cause. All but four of the patients were white. He questioned the extent of the decreased incidence of syphilitic abdominal aneurysms, citing the frequent absence of histologic proof in past reviews and the relative preponderance of Negroes in some. Three-fourths of the syphilitic abdominal aortic aneurysms have been found in patients under 50 years of age. Less than 5 per cent have occurred in patients over 60 years of age. The majority of the patients are male, and Negroes are predominantly affected.

Pathology. Characteristically, the aorta is segmentally involved by the syphilitic inflammatory and destructive process. At such local or segmental regions of aortitis, destruction of the muscle fibers and of the elastic elements of the media leads to weakening of the wall and dilatation. Ultimately the intima and adventitia are involved in the weakening process. The additive influence of the increase in systolic blood pressure, especially when hypertension is present, results in progressive outpouching and the formation of one or more saccular aneurysms. Less frequently a large portion (or the entire length) of the thoracic aorta dilates, forming a *fusiform aneurysm*. The wall of the aneurysmal sac becomes a thinned-out collagenous membrane with fibrous adhesion of the adventitia to neighboring structures. The cavity becomes lined and partially occupied by a *laminated thrombus*. The major complications arise from pressure upon, and perforation into, adjacent thoracic structures. An aneurysm lined by a laminated clot may cease to progress and may remain asymptomatic for years. One or more of the sinuses of Valsalva may be the site of an aneurysm, not necessarily associated with one of the ascending aorta. Of the large branches of the aorta, the innominate artery most often dilates to

dullness extends beyond that of the normal right atrial border. Dilatation of the arch may give rise to upper retromanubrial dullness. Other conditions, such as thyroid enlargement and mediastinal neoplasm, may also be responsible for similar abnormal percussion findings.

Increased visible and palpable pulsations in the upper parasternal intercostal spaces and in the suprasternal notch may be detected with moderate aortic dilatation. However, similar pulsations occur without roentgen evidence of aortic dilatation. Of the abnormal physical signs described above, this is probably the least dependable.

Roentgen Examination. The only reliable method for the clinical detection of lesser degrees of aortic dilatation is roentgen examination utilizing films taken in several positions, fluoroscopy, and when feasible, angiocardiography. The characteristic findings are *convex prominence* and *increased pulsations of the ascending aorta.* As a diagnostic aid during the latent stage of syphilitic aortitis, conventional PA roentgenograms have not proved to be valuable. Such films of 200 syphilitics between 20 and 50 years of age and of 200 normal individuals of the same age group were found, with few exceptions, to have identical aortic measurements (Boharas et al.) Films made in the oblique positions, especially the LAO, are more informative as to abnormal measurements of the ascending aorta The impression of the aortic arch upon the barium-filled esophagus may be measured. Normally, in adults below the age of 40, the aortic arch impression is less than 3 cm

Fluoroscopic study of the heart and aorta with the patient turned to various positions may reveal *exaggerated pulsations of the aorta* even in the absence of evidence of dilatation on the roentgen film Fluoroscopic estimation of the width of the aorta, particularly of the ascending portion, and of the character of its pulsations depends upon the fluoroscopist's personal experience with patients of all age groups. The diameter of the ascending aorta increases with age

Angiocardiography yields the only reliable information as to the diameter of the aorta in the living patient. The root or lower ascending portion of the aorta, the site of predilection for aortic syphilis, is obscured in the PA roentgenogram but is visible in the angiocardiogram. Steinberg et al., employing angiocardiography, demonstrated that the diameter of the midascending aorta varies normally from 16 to 38 mm and that the aortic diameters diminish progressively distally. In 60 patients with syphilitic aortitis, the diameter of the midascending aorta was above normal in all, averaging 45.4 mm.

Other roentgen alterations regarded as diagnostic of syphilitic aortitis are *irregularity* of the aortic lumen, *increased density* of the aortic shadow, and *calcification of the wall* of the ascending aorta. Calcium deposition in the aorta is most often seen roentgenographically in the aortic knob as a manifestation of atherosclerosis in older patients. *Calcification of the ascending aorta, however, is unusual.* In syphilitic aortitis, on the other hand, this roentgen finding has been observed in 18 to 22 per cent of cases, the calcium deposits varying from thin linear plaques to extensive calcification of the walls of the ascending aorta. Calcification is *not* an early sign of syphilitic aortitis and is due to superimposed atherosclerosis.

Roentgen evidence of aortic dilatation and increased localized pulsations not only occurs as a result of syphilitic aortitis but may also be associated with hypertension, atherosclerosis of the aorta, aortic valve insufficiency, coarctation of the aorta, and other less common conditions Evaluation of such findings must take into consideration the age of the patient, history of early syphilis, specific serologic reactions, and evidence of other stigmas present in syphilis

STENOSIS OF THE OSTIA OF BRANCHES OF THE AORTA

The ostia of the principal branches of the thoracic aorta may be so narrowed as to be completely obstructed by the syphilitic inflammatory process. The ostia of the coronary arteries, one or both, are most frequently affected. Stenosis is due to encroachment by elevated intimal plaques Coronary ostia stenosis may exist as a single complication of syphilitic aortitis or may be associated with dilatation or aneurysm of the root of the aorta and with aortic valve deformity. The orifices of the innominate, left common carotid, and left sub-

if ever, is superimposed on an aortic valve deformed by syphilis alone. The syphilitic pathologic alterations of the leaflets, unlike those of rheumatic valvulitis, do not favor bacterial surface infection. When the latter occurs, *a third factor, usually rheumatic valvulitis, is present.* In the five cases of associated cardiovascular syphilis and bacterial endocarditis cited by Koletsky, stigmas of rheumatic heart disease were demonstrated unequivocally in four, and there was combined syphilitic and rheumatic aortic valvular disease in at least two. The rheumatic valvular lesion may be slight or obscured and easily overlooked.

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Symptoms. The clinical course is divisible into two phases, an asymptomatic and a symptomatic. As many as one-half of the patients with syphilitic aortic insufficiency have no cardiorespiratory symptoms when the lesion is first detected. Some may be conscious only of *palpitation* or of *blood vessel pulsations* in the head and extremities. The duration of the asymptomatic phase is variable and is influenced by many factors, such as the degree of valvular incompetence, the state of myocardial nutrition, and the patient's occupation. McDermott et al reported this phase as being of 2 to 10 years duration, and averaging 3.5 years. In a series studied by Montgomery, predominantly of Negroes who had received little or no treatment, the average duration in the majority was 6 months or less, the longest being 3 years in one patient, and 6 months in two Compensation for the valvular defect is maintained until the hypertrophied left ventricular muscle fails to receive adequate nourishment because of reduced coronary flow, secondary to lowering of the diastolic pressure and to concomitant coronary ostia stenosis or, in those patients over 50 years of age, to coronary arteriosclerosis

The characteristic symptoms are those of left ventricular failure *Dyspnea* is the most frequent, at first *on exertion*, and later *at rest*. With increasing pulmonary vascular engorgement, *orthopnea* and *cough* appear Recurring episodes of *paroxysmal nocturnal dyspnea* and *acute pulmonary edema* are common Eventually, symptoms of right ventricular failure develop, with systemic venous engorgement, dependent edema, serous effusions, and tenderness and enlargement of the liver Not uncommonly the onset of the symptomatic phase is acute and dramatic The patient, who had previously been engaged in even arduous labor without cardiorespiratory embarrassment, is suddenly and precipitously incapacitated by acute pulmonary edema followed by progressive congestive heart failure In general, the response to treatment for congestive failure is less satisfactory than it is in patients in whom hypertension or rheumatic heart disease is the cause. Marked congestive failure may respond well to digitalis, diuretics, and sodium restriction for a relatively short time, but eventually, with progressive myocardial exhaustion, these measures become ineffective. The average duration of life, when severe failure is present, is 1 to 1.5 years. However, patients with milder symptoms may maintain compensation with treatment and continue to work for as long as 10 to 14 years after the onset of symptoms.

Pain is another frequent symptom in patients with aortic insufficiency due to syphilis Precordial pain, present in 20 to 30 per cent of the cases, is usually due to the coexistence of coronary ostia stenosis. In older patients, coronary arteriosclerosis may be responsible. Pain of a more persistent character may arise from the compression effects of an associated aortic aneurysm.

Physical Signs. The presence of aortic insufficiency cannot be ascertained without the detection of an *early-diastolic blowing high-pitched murmur.* This is best heard over the anatomic position of the aortic valve in the region of the *3d or 4th left intercostal space near the sternal border.* The quality and intensity of the murmur vary with the degree of valvular incompetence. It may be very soft and audible only when the patient is sitting forward and during full expiration. It may be loud and blowing and transmitted to the region of the apex Occasionally, the early-diastolic blowing murmur is heard *only at the apex.* If the ascending aorta dilates, the murmur is heard farther to the right of the sternum The aortic 2d sound may be normal or accentuated, but with increasing dilatation of the aortic ring and deformity of the cusps, it diminishes in intensity

Three additional murmurs may be identified in patients with syphilitic aortic insufficiency. If the root of the aorta is dilated, a *harsh systolic murmur* is audible to the right of the upper sternum and over the carotid arteries. This murmur, in conjunction with a diminished or absent aortic 2d sound, may suggest the presence of organic aortic stenosis. The latter lesion, however, cannot possibly occur from syphilitic deformity of the valve. When it is present, concomitant rheumatic valvulitis or calcification of the ring or cusps is responsible. In Woodruff's series, 7.3 per cent of necropsied cases of syphilitic aortic insufficiency exhibited calcification of the aortic valve.

With progressive dilatation of the left ventricle and of the mitral ring, a *blowing systolic murmur* is heard *at the apex* of the heart and in the axilla. It represents a relative mitral

from localized rupture of the abdominal aneurysm and the formation of a false aneurysm, with exposure of the spinal nerve to the pulsating wall or the blood stream. Renal colic may follow kidney displacement and ureteral compression Anorexia, nausea, and vomiting from pressure on the gastrointestinal structures are other symptoms which may occur with abdominal aneurysm

Physical Signs. These vary with the portion of the aorta predominately involved and with the adjacent structures compressed. A deep-seated aneurysm, even one of large dimensions, may exhibit no detectable abnormal physical changes The heart remains normal in size despite the presence of an aneurysm larger than the heart itself, unless other cardiovascular lesions are present

Saccular aneurysms of the ascending aorta and of the arch produce many detectable physical alterations of the thorax, head, neck, and upper extremities Visible and palpable localized pulsations may be noted in the 2d and 3d interspaces and in the suprasternal notch. Marked pulsations in the right supraclavicular region are produced by an *innominate artery aneurysm* With each heart beat, the anterior chest wall may be displaced anteriorly, and a *diastolic shock may be palpable* *Infrequently*, a pulsating tumor points on the anterior chest wall Percussion outlines the borders of the aneurysm unless the thorax is markedly emphysematous or the aneurysm is deep seated A dull or flat percussion noted over the upper sternum is elicited with aneurysms of the arch Over the right upper parasternal area, *a systolic murmur* and *thrill* are usually present The murmur is rough and is transmitted to the carotid arteries *Compression of the superior vena cava* is evidenced by edema, cyanosis, and engorgement of the veins of the face, neck, and upper extremities Ocular manifestations, in addition to *Argyll-Robertson pupils*, include *dilatation* of the right pupil and *Horner's syndrome* from stimulation or destruction of the cervical sympathetic nerves, respectively As the systolic expansion of an aneurysm of the descending aortic arch displaces the left main bronchus downward, the tracheal and cricoid cartilages are visibly or palpably tugged in the same direction (*tracheal tug*) *Inequality of the pulse volume and pressure* of the arteries of the upper extremities represent either stenosis of the ostia or incorporation of the proximal portions of the innominate or left subclavian arteries by the aneurysm.

Aneursyms of the descending thoracic aorta expand into the posterior portion of the left thorax. If the aneurysmal sac is large, visible pulsations are noted in the left infrascapular region. Left paravertebral dullness and a systolic murmur over the left posterior thorax may also be detected

A *syphilitic abdominal aneurysm* is manifested physically by a pulsating mass in the epigastrium, left hypochondrium, or lumbar region. Over the mass, a *thrill* and a *bruit* may be found. Arterial pulsations of the lower extremities may be diminished. Arteriosclerotic abdominal aortic aneurysms, the major lesion to be differentiated, occur most frequently in patients over 60 years of age, and rarely before 50 The aorta below the origin of the renal arteries is then predominantly involved. The aneurysms are usually fusiform, which tends to dilute eroding pressure so that vertebral bone erosion does not occur Symptoms are noted late and may be absent in about one-third of the cases. Rupture may be responsible for the initial symptoms.

PULMONARY ARTERY COMPRESSION. Stenosis *of the lumen of the pulmonary artery from* compression by aneurysms arising from the sinuses of Valsalva, or from the concave surface of the root of the ascending aorta, and bulging anteriorly and to the left, may lead to dilatation and hypertrophy of the right ventricle and the clinical syndrome of *cor pulmonale* This complication is uncommon, only 88 cases have been found in the literature between 1811 and 1951 by Pearson and Nichol In the past, few have been diagnosed during life, recently, however, definitive diagnosis has been accomplished in suspected cases by means of cardiac catheterization and angiocardiography

The clinical picture is variable In some, the aneurysm is silent, and the predominant symptoms are those of gradually progressing or acutely recurring episodes of right heart failure, manifested by dyspnea, cyanosis, systemic venous engorgement, hepatomegaly, ascites, peripheral edema, and electrocardiographic evidence of right heart strain In patients with aneurysm and aortic insufficiency, the condition is suspected when the ECG re-

tension, as well as with rheumatic heart disease and bacterial endocarditis. Diagnostic difficulties arise, especially when standard serologic reactions are negative and when there is heart failure with atrial fibrillation.

Aortic insufficiency caused by atherosclerosis plus hypertension in patients beyond 60 years of age is not unusual. Extensive atherosclerosis of the ascending aorta is the principal predisposing factor. Hypertension per se rarely causes aortic insufficiency, when it does, the *incompetence* of the dilated valve *ring* is transient and unaccompanied by peripheral vascular signs. It subsides following reduction of the blood pressure. *Intimal tears* of the aorta just above the commissures may be followed by scarring and widening of the commissures and ptosis of the leaflets of the valve. Less frequently, *chronic dissecting aneurysms* may result in the same phenomenon. The clinical diagnosis may be entertained when, in a known hypertensive patient with negative serologic reactions for syphilis, aortic insufficiency develops subsequent to an acute episode of chest pain and dyspnea

Calcification of the aortic ring and cusps, secondary to marked atherosclerosis of the aortic valve, may lead to insufficiency and stenosis The insufficiency is most often not marked, the aortic 2d sound tends to be diminished or absent, and the peripheral manifestations are only moderate. However, free aortic regurgitation and its attendant peripheral vascular phenomena may occur Syphilitic aortic insufficiency and calcific aortic valve disease may coexist Woodruff reported the presence of calcification of the ring and cusps in over 7 per cent of his group of syphilitics with aortic insufficiency In some patients, there was sufficient calcification to produce valvular stenosis, even though the commissures were widened

In younger patients with aortic insufficiency, the differentiation between syphilitic aortitis and rheumatic endocarditis as the cause may present clinical diagnostic problems Several factors may be responsible for difficulties in the differential diagnosis. In either disease, a history of infection, other physical stigmas, and positive serologic reactions may be lacking Under such circumstances, the absence of aortic dilatation or precordial pain in a syphilitic, and of mitral stenosis in a rheumatic, patient are additional obstacles. Also, the presence of a mid-diastolic rumbling murmur at the apex requires differentiation between relative and organic mitral stenosis Patients with acquired mitral stenosis exhibit all or several of the associated features of the latter lesion. These include the presystolic thrill, the accentuated 1st apical and 2d pulmonic sounds, and enlargement of the pulmonary artery-conus region and the left atrium. In the presence of congestive failure, there is a better response to therapy, a relatively longer survival period after the onset of failure, and the frequent occurrence of atrial fibrillation Additional support for the diagnosis of acquired mitral stenosis includes a history of rheumatic fever, positive immune blood reactions indicating current or recent streptococcal infection, and electrocardiographic alterations of combined or predominant right heart strain.

The *coexistence of rheumatic heart lesions in patients with cardiovascular syphilis* has been reported to occur in 1 to 10 per cent. Of 135 cases of syphilitic heart disease studied by Koletsky, 24 (or 18 per cent) had rheumatic heart disease. Three major combinations of lesions have been described. There may be syphilitic aortic insufficiency and rheumatic involvement of the mitral, tricuspid, and pulmonic valves, singly or in combination; syphilitic aortitis and rheumatic *aortic valve* deformity, or coexisting syphilitic and rheumatic aortic valvulitis. Other lesions of either infection, such as rheumatic myocarditis and coronary ostia stenosis, may also be present.

SYPHILITIC AORTIC INSUFFICIENCY AND BACTERIAL ENDOCARDITIS

The combination of these two diseases is of infrequent occurrence. Wright and Zeck reviewed the literature up to 1940 and reported the incidence of syphilitic aortitis in 1.3 per cent of 1,255 cases of bacterial endocarditis Five cases of combined syphilitic heart disease and bacterial endocarditis were found by Koletsky in 4,000 autopsies. It is generally accepted that the mere presence of syphilitic aortitis does not predispose *the aortic* valve to bacterial implantation. While acute bacterial endocarditis may occasionally involve a normal aortic valve in patients *with* syphilitic aortitis, subacute bacterial endocarditis rarely,



Fig. 9-6. Aneurysms of the thoracic aorta. A Of the ascending aorta B. Of the transverse segment of the arch. C. Of the descending thoracic aorta.

be displaced downward or to the left by a large aneurysm *Calcium deposition in the walls* is common, and its presence is of aid in the differentiation between aneurysm and other mediastinal tumors An innominate artery aneurysm appears as an oval or semicircular mass extending to the right and upward, behind and above the right clavicle. The *trachea may be displaced to the left. Aneurysms of the convex portion of the ascending* aorta extend anteriorly and into the right lung field. The heart may be displaced leftward, and the sternum or ribs may be eroded Those of the arch compress and displace the trachea and esophagus posteriorly The LAO view may reveal *narrowing* of the left main bronchus by an aneurysm of the descending portion of the arch *Fusiform aneurysms* of the descending thoracic aorta are best visualized in oblique or lateral views, *saccular aneurysms* project into the left lung field Syphilitic aneurysms of the abdominal aorta are often not discernible in the ordinary film of the abdomen Calcium deposits in the wall aid in the delineation The cardiac portion of the barium-filled stomach may be seen *displaced forward* and to the left With erosion of vertebral bodies, the polycyclic contour of the affected segment is best seen in lateral and oblique views. The anterior and lateral portions of the vertebral bodies are eroded, but the intervertebral disks are spared



Fig 9-7. Aneurysms of the thoracic aorta A. Of the descending aorta. B Of the arch (larger than the heart).

aneurysmal proportion, either as a single such lesion, or as part of an aneurysm of the ascending aorta and the arch.

Two forces determine the main direction of expansion of an aneurysm: the systolic impact of the blood stream and gravity. *Aneurysms of the ascending aorta* enlarge anteriorly, upward and to the right, impinging upon the second and third ribs, the right lung and bronchus, the superior vena cava, and the pulmonary artery. *Aneurysms of the arch* occupy a horizontal position and may compress the trachea, esophagus, left bronchus, and the recurrent laryngeal, the cervical sympathetic, and occasionally, the left phrenic nerves; they also may erode the sternum. *With involvement of the descending thoracic aorta,* the aneurysm expands downward and backward toward the left posterior thoracic wall and may erode the vertebral bodies. *Syphilitic abdominal aneurysms,* located above the renal arteries, displace the stomach, duodenum, colon, left ureter and may irritate spinal nerve roots or erode the bodies of the lower thoracic vertebrae Aneurysms of the sinuses of Valsalva may become quite large and exert pressure similar to those of the proximal ascending aorta, they may compress the pulmonary artery or conus and the right atrium or ventricle. *Innominate aneurysms* displace the trachea to the left and may erode the medial portion of the right clavicle.

Aneurysms of the ascending aorta are associated with aortic insufficiency in 20 per cent of the cases. The presence of an aneurysm has no influence upon the subsequent occurrence of aortic valve insufficiency. On the other hand, it is not common for an aneurysm to evolve after aortic insufficiency of appreciable degree exists. *Abdominal aortic aneurysms* are located at or above the origin of the renal arteries and are most often saccular. *In Scott's series,* 34 *per cent* were associated with thoracic aneurysms and 18 per cent with aortic insufficiency. Erosion of vertebral bodies and compression of spinal nerve roots are frequent complications Atherosclerosis and calcification of the aneurysmal wall are usually concomitant.

Clinical Course. Several factors influence the clinical course of syphilitic aneurysms It is questionable whether antisyphilitic therapy exerts a favorable influence in retarding or arresting progression Deep-seated, nonprogressive aneurysms may remain silent and undetected for years. Aortic insufficiency, coronary ostia stenosis, and concomitant coronary arteriosclerosis and hypertension shorten the survival period. Serious secondary clinical syndromes develop from compression of such structures as the superior vena cava, pulmonary artery, and left main bronchus Erosion and rupture into adjacent thoracic organs usually terminate the clinical course immediately. However, some patients do survive for prolonged periods after the rupture.

Symptoms. *Pressure phenomena* are primarily responsible for the symptoms of thoracic aortic aneurysms. Precordial pain and symptoms of heart failure, when present, are manifestations of other associated cardiovascular lesions. The most troublesome symptoms are *cough* and *pain.* Cough is the earliest and most frequent symptom because the opportunity for compression, displacement, and erosion of respiratory structures is everywhere present. Compression atelectasis of the lung and pressure on the trachea and the main bronchi (especially of the left) produce a dry cough Marked stenosis of the left main bronchus by an aneurysm of the descending portion of the arch may lead to *pulmonary atelectasis,* followed by infection, bronchiectasis, hemoptysis, recurring episodes of bronchopneumonia, and pulmonary abscess. The latter clinical complex has been termed "aneurysmal pthisis" *Hemoptysis* may also result from erosion of the trachea and bronchi. The cough may have a "brassy" quality as a result of compression of the trachea or bronchi. Pain is the result of erosion of ribs, sternum, and vertebral bodies and of nerve root irritation. Pressure upon the brachial plexus by an innominate artery aneurysm produces pain about the right shoulder and in the right upper extremity. *Left vocal cord paresis or paralysis,* due to recurrent laryngeal nerve involvement, causes *hoarseness. Dyspnea* results from tracheal or bronchial narrowing, and inspiratory *stridor* is experienced when the trachea is displaced and stenosed. *Dysphagia* from esophageal displacement and compression occurs infrequently. Phrenic nerve irritation may lead to annoying *hiccough* The clinical syndrome of *cor pulmonale* may evolve from compression of the pulmonary artery or conus and of the right heart chambers. Aneurysms of the descending aorta may become very large before symptoms are noted.

Pain is the most common and severe symptom of syphilitic abdominal aneurysms. It is often throbbing, worse at night, and relieved by position change. Severe pain may result



Fig 9-6 Aneurysms of the thoracic aorta. A. Of the ascending aorta. B. Of the transverse segment of the arch C Of the descending thoracic aorta.

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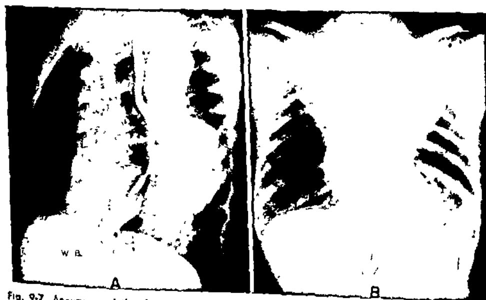


Fig. 9-7. Aneurysms of the thoracic aorta A Of the descending aorta. B. Of the arch (larger than the heart).

aneurysmal proportion, either as a single such lesion, or as part of an aneurysm of the ascending aorta and the arch.

Two forces determine the main direction of expansion of an aneurysm: the systolic impact of the blood stream and gravity. *Aneurysms of the ascending aorta* enlarge anteriorly, upward and to the right, impinging upon the second and third ribs, the right lung and bronchus, the superior vena cava, and the pulmonary artery. *Aneurysms of the arch* occupy a horizontal position and may compress the trachea, esophagus, left bronchus, and the recurrent laryngeal, the cervical sympathetic, and occasionally, the left phrenic nerves; they also may erode the sternum. *With involvement of the descending thoracic aorta,* the aneurysm expands downward and backward toward the left posterior thoracic wall and may erode the vertebral bodies. *Syphilitic abdominal aneurysms,* located above the renal arteries, displace the stomach, duodenum, colon, left ureter and may irritate spinal nerve roots or erode the bodies of the lower thoracic vertebrae. Aneurysms of the sinuses of Valsalva may become quite large and exert pressure similar to those of the proximal ascending aorta; they may compress the pulmonary artery or conus and the right atrium or ventricle. *Innominate aneurysms* displace the trachea to the left and may erode the medial portion of the right clavicle.

Aneurysms of the ascending aorta are associated with aortic insufficiency in 20 per cent of the cases. The presence of an aneurysm has no influence upon the subsequent occurrence of aortic valve insufficiency. On the other hand, it is not common for an aneurysm to evolve after aortic insufficiency of appreciable degree exists *Abdominal aortic aneurysms* are located at or above the origin of the renal arteries and are most often saccular. In Scott's series, 34 per cent were associated with thoracic aneurysms and 18 per cent with aortic insufficiency Erosion of vertebral bodies and compression of spinal nerve roots are frequent complications Atherosclerosis and calcification of the aneurysmal wall are usually concomitant.

Clinical Course. Several factors influence the clinical course of syphilitic aneurysms It is questionable whether antisyphilitic therapy exerts a favorable influence in retarding or arresting progression Deep-seated, nonprogressive aneurysms may remain silent and undetected for years. Aortic insufficiency, coronary ostia stenosis, and concomitant coronary arteriosclerosis and hypertension shorten the survival period. Serious secondary clinical syndromes develop from compression of such structures as the superior vena cava, pulmonary artery, and left main bronchus. Erosion and rupture into adjacent thoracic organs usually terminate the clinical course immediately. However, some patients do survive for prolonged periods after the rupture

Symptoms. Pressure phenomena are primarily responsible for the symptoms of thoracic aortic aneurysms. Precordial pain and symptoms of heart failure, when present, are manifestations of other associated cardiovascular lesions. The most troublesome symptoms are *cough* and *pain.* Cough is the earliest and most frequent symptom because the opportunity for compression, displacement, and erosion of respiratory structures is everywhere present. Compression atelectasis of the lung and pressure on the trachea and the main bronchi (especially of the left) produce a dry cough. Marked stenosis of the left main bronchus by an aneurysm of the descending portion of the arch may lead to *pulmonary atelectasis,* followed by infection, bronchiectasis, hemoptysis, recurring episodes of bronchopneumonia, and pulmonary abscess The latter clinical complex has been termed "aneurysmal pthisis." *Hemoptysis* may also result from erosion of the trachea and bronchi The cough may have a "brassy" quality as a result of compression of the trachea or bronchi. Pain is the result of erosion of ribs, sternum, and vertebral bodies and of nerve root irritation. Pressure upon the brachial plexus by an innominate artery aneurysm produces pain about the right shoulder and in the right upper extremity. *Left vocal cord paresis or paralysis,* due to recurrent laryngeal nerve involvement, causes *hoarseness. Dyspnea* results from tracheal or bronchial narrowing, and inspiratory *stridor* is experienced when the trachea is displaced and stenosed *Dysphagia* from esophageal displacement and compression occurs infrequently. Phrenic nerve irritation may lead to annoying *hiccough.* The clinical syndrome of *cor pulmonale* may evolve from compression of the pulmonary artery or conus and of the right heart chambers Aneurysms of the descending aorta may become very large before symptoms are noted

Pain is the most common and severe symptom of syphilitic abdominal aneurysms It is often throbbing, worse at night, and relieved by position change. Severe pain may result

tively long period *Survival up to 3 years* has followed rupture into the pulmonary artery, the superior vena cava, and the right heart chambers These structures are infrequently eroded, but the resultant clinical syndromes are dramatic and interesting

RUPTURE INTO HEART CHAMBERS, PULMONARY ARTERY, AND SUPERIOR VENA CAVA. The clinical features are related to the site and size of the communication and to phenomena associated with the structure eroded *Chest pain, dyspnea,* and varying degrees of *shock* are the usual immediate symptoms The rupture is frequently preceded by strenuous or increased physical exertion

RUPTURE INTO THE SUPERIOR VENA CAVA England, and later Franklin, reviewed 125 cases reported since the first was published in 1833 At the time of rupture, the patient experiences moderate *dyspnea, chest pain,* and *a sense of heat* in the upper part of the body These symptoms are accompanied by rapid *venous distention, swelling,* and *cyanosis* of the face, neck, arms, and upper chest A *loud continuous murmur* and *a systolic thrill* are detected at the aortic area, and peripheral signs of an arteriovenous shunt develop Aortic insufficiency is usually not present One patient is reported to have survived for 526 days Since the clinical diagnosis is readily made, cardiac catheterization or angiocardiography add little necessary information England reported an unsuccessful attempt to close the communication

RUPTURE INTO THE PULMONARY ARTERY Nicholson found 81 cases in the literature since 1812 Only four of them were diagnosed during life He added two which were diagnosed antemortem The aneurysms arise from the *ascending aorta or the sinuses of Valsalva* in 85 per cent of the patients In some cases, manifestations of pulmonary artery compression and stenosis may precede the rupture In addition to chest pain, the patient experiences *dyspnea* and *cough* from pulmonary vascular congestion The signs of right heart failure progress rapidly At the pulmonic area, murmurs and thrills (similar to those of patent ductus arteriosus) appear, and peripherally the signs of an arteriovenous shunt are seen Roentgen examination reveals in some patients, in addition to cardiomegaly and the aneurysm, dilatation of the pulmonary artery–conus region and pulmonary vascular engorgement The *ECG* may eventually indicate right or combined right and left ventricular hypertrophy. Cardiac catheterization reveals findings similar to those of patent ductus arteriosus. The clinical course depends upon the size of *the communication.* If it is small, the patient may survive for months.

RUPTURE INTO RIGHT HEART CHAMBERS. In rare instances, the right atrium or ventricle is perforated by syphilitic aneurysms of the root of the ascending aorta or the sinuses of Valsalva Congenital aneurysms of the sinuses are more prone to rupture into the right heart chambers Oram collected 21 reported cases in which some of the patients survived for several months following sinus aneurysm perforation. Severe pain in the chest and upper abdomen, frequently following exertion, persists for several hours If the patient survives, there is a latent asymptomatic period averaging a few weeks, succeeded by increasing dyspnea and progressive and fatal right heart failure, with manifestations secondary to the shunt and tricuspid insufficiency *Murmurs* and *thrills,* like those of patent ductus arteriosus, are noted in almost all the cases and are located near the center or slightly to the left of the sternum in the 2d to 4th interspace In *patients with rupture into the right atrium,* the murmurs (especially the diastolic) are transmitted along the right sternal border down to the liver and umbilicus Paroxysmal atrial tachycardia and fibrillation are common. When the shunt is into the right ventricle, pressure necrosis and perforation of the interventricular septum may occur.

RUPTURE OF ANEURYSMS OF THE ABDOMINAL AORTA Hemorrhage into the retroperitoneal space or into the peritoneal cavity is the usual consequence of rupture of an abdominal aneurysm. Death may be delayed for several hours or days, allowing opportunity for surgical repair. Less *commonly, rupture* occurs into the gastrointestinal tract and is followed by rapid exsanguination.

ELECTROCARDIOGRAPHIC CHANGES

No specific or characteristic alterations have been described. Transient T-wave and other minor changes may occur during the primary and secondary phases, which have been attributed by some to the effect of therapy. Steiger et al. studied 30 patients with early syphilis, 15 of whom exhibited transient

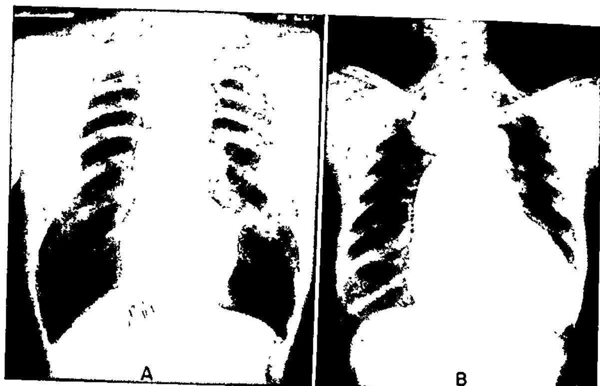


Fig. 9-4. A. Calcification of the ascending aorta in a male Negro with clinical manifestations of stenosis of the orifices of the innominate and left common carotid arteries. B. Calcification of the dilated ascending aorta Aneurysm of the innominate artery is present.

veals evidence of either right or combined right and left ventricular hypertrophy However, electrocardiographic clues are not always present. The local physical signs, often absent early, are noted *at the pulmonic area* where a *systolic murmur* develops. In some cases, there may be an associated *thrill* and *diastolic murmur* The clinical course is that of progressive and fatal *right heart failure* The latter may be acutely accelerated by rupture of the aneurysm through the eroded wall of the pulmonary artery.

Roentgen Examination. Except for aneurysms of the sinuses of Valsalva and small outpouchings from the concave aspect of the arch, *thoracic aortic aneurysms* are readily discerned in PA and oblique roentgen films (Figs. 9-4 to 9-8). They appear as dense, sharply defined, and usually smooth convex projections from the upper mediastinum or the normal vascular pedicle into the lung fields. In the absence of other cardiovascular lesions, especially aortic insufficiency and hypertension, the heart is not enlarged. It may



Fig. 9-5. Aneurysms of the thoracic aorta A. Of the ascending aorta. B. Of the ascending aorta, associated with marked left ventricular enlargement secondary to aortic insufficiency. C. Of the innominate artery.

the results of therapy in 743 cases of syphilis followed for at least 10 years Cardiovascular syphilis was found to have appeared in 27.6 per cent of those who had received little or no specific therapy. The incidence was 13 9 per cent in patients treated inadequately. No late lesions were detected in 114 patients given adequate treatment Of 241 patients followed by Thompson et al for 15 to 25 years after treatment for early syphilis, only 18 had definite lesions, and 17 of these patients had had inadequate therapy. Maynard and Lingg found cardiovascular syphilis five times more frequent in the absence of specific treatment and concluded that the incidence varied inversely with the amount of treatment received.

The spirochetocidal effect of penicillin was demonstrated by Mahoney et al in 1943 Wide experience since then has yielded convincing evidence that penicillin, administered during the early phase of the infection, reduces the incidence of syphilitic aortitis Approximately 85 to 90 per cent of patients with early syphilis are cured by penicillin The cure rate for primary seronegative syphilis is 90 to 98 per cent, for primary seropositive 85 to 90 per cent, and for secondary syphilis 75 to 85 per cent Adequate effective penicillin therapy is afforded by 6,000,000 units administered intramuscularly in the form of either *crystalline procaine penicillin G in oil* with 2 per cent aluminum monostearate given in doses of 600,000 units twice weekly for 5 weeks or as *procaine penicillin in aqueous suspension* given in doses of 600,000 units daily for 10 days

Past experience with metal therapy has indicated that the development of late lesions may be prevented in patients in whom the disease is detected and treated during the latent phase Although a decade or more must elapse before final evaluation of the preventive effectiveness of penicillin therapy during this stage of syphilis, the results to date are highly favorable Although patients treated during the early latent period (less than 3 years after the primary lesion) are less likely to obtain biologic cure, the development of late manifestations are almost always prevented Those treated during the late latent period (more than 3 years after infection) rarely are cured, but the disease may be arrested before late lesions evolve.

There is no uniformity of opinion as to whether spirochetocidal therapy is effective after aortic insufficiency or aneurysm has developed The objectives sought are arrest or retardation of the pathologic alteration, relief of symptoms, and prolongation of life. Padget and Moore treated such patients with heavy metals and reported approximate doubling of the life span. Kampmeier and Coombs found that neither the kind or the amount of antisyphilitic therapy altered the course in 163 patients with aortic insufficiency. Barnett and Small critically reviewed previous reports of the effectiveness of treatment for patients with late cardiovascular syphilitic lesions and pointed to errors in statistic analysis. From careful statistic analysis of the results of specific therapy with both heavy metals and penicillin in 334 cases with aortic insufficiency, aneurysm, or both, they concluded that specific therapy probably improves prognosis to some degree at any phase of cardiovascular syphilis, that effectiveness consistently diminishes as the disease has progressed; that therapy is effective when administered before the symptomatic phase of late lesions; that therapy is of doubtful value after the onset of symptoms; and that, when advanced heart failure exists, therapy "has lost a great deal of its value" Penicillin is well tolerated during all stages, even in the presence of congestive failure. The early fears of serious *Jarisch-Herxheimer reactions* and of therapeutic paradox have been dispelled From 10 to 20 million units of penicillin may be given Favorable effect from penicillin has been observed in patients with paroxysmal nocturnal dyspnea, precordial pain, and congestive failure. In the latter instance, the usual measures for the treatment of heart failure are also employed A reduction of the intensity of the aortic diastolic murmur has been noted in some cases following penicillin administration

Surgical Treatment of Syphilitic Aneurysms. During the past decade, great strides have been made in the surgical treatment of aortic aneurysms Treatment has been primarily applied to aneurysms of the abdominal aorta, the great majority of which are of arteriosclerotic origin The problem of syphilitic aneurysm is rapidly receding into the past, whereas that of the arteriosclerotic aneurysm is of future importance.

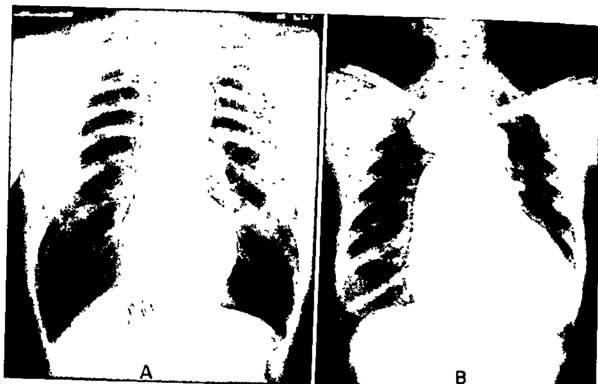


Fig. 9-4. A. Calcification of the ascending aorta in a male Negro with clinical manifestations of stenosis of the orifices of the innominate and left common carotid arteries. B. Calcification of the dilated ascending aorta. Aneurysm of the innominate artery is present.

veals evidence of either right or combined right and left ventricular hypertrophy. However, electrocardiographic clues are not always present The local physical signs, often absent early, are noted *at the pulmonic area* where a *systolic murmur* develops. In some cases, there may be an associated *thrill* and *diastolic murmur*. The clinical course is that of progressive and fatal *right heart failure*. The latter may be acutely accelerated by rupture of the aneurysm through the eroded wall of the pulmonary artery

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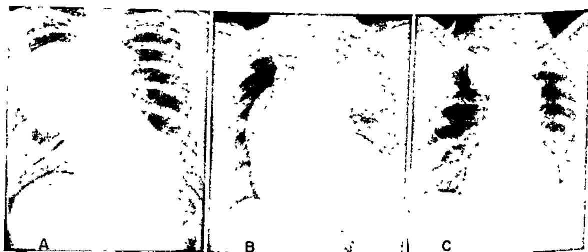


Fig. 9-5. Aneurysms of the thoracic aorta. A. Of the ascending aorta. B. Of the ascending aorta, associated with marked left ventricular enlargement secondary to aortic insufficiency. C. Of the innominate artery.

3

Graphic data in aortic aneurysms

ALDO A. LUISADA

The great majority of the aneurysms of the aortic arch are syphilitic, while most of those of the abdominal aorta are caused by an atherosclerotic lesion. The aneurysm may be fusiform or saccular The blood contained in the pouch may remain fluid, in such a case, the aneurysm acts like a reservoir which dilates during systole and shrinks with diastole In many cases, however, stratified thrombi fill the pouch, which behaves like a solid mass Compression of one or more arteries is possible and may lead to unilateral or bilateral disappearance of the radial pulse

When the aneurysm grows outward, it forms a mass having an expansive pulsation In certain cases, the systolic thrust of the apex is followed by a diastolic thrust due to the recoil of a retrocardiac aneurysm (*double pulsation*) Auscultation of the mass reveals the heart sounds and *a double murmur*, caused by the blood entering and leaving the pouch through a narrow opening

PULSE TRACINGS. CARDIOGRAM

Severe changes of circulatory dynamics take place when the aneurysmal sac is large, elastic, and contains fluid blood, if the opening is narrow, the effects are more marked The sac behaves like a *reservoir* because it fills during systole, decreasing the systolic pressure below it, and gives back the blood in diastole, increasing the diastolic pressure below it Therefore, a comparison between an artery above and one below the sac reveals that the pulse is smaller and has a slower rise (*pulsus tardus*) in the arteries placed below.

In *aneurysm of the ascending aorta*, a high but slowly developing pulsation is recorded over the 2d and 3d right interspace, where the pouch contacts the soft parts of the anterior chest wall The apex cardiogram may reveal a double thrust (one in systole, one in diastole) or only a diastolic thrust due to the rebound of the aneurysm which displaces the entire heart. The tracings of the brachial arteries reveal *a simultaneous rise of the two* pulses, however, the *right pulse is smaller than the left* and has a slower rise, so that its peak is delayed (Fig 9-9A).

In *aneurysm of the aortic arch*, a typical, high, and slow pulsation is recorded at the suprasternal notch The brachial pulses have a simultaneous rise, but *the left pulse is smaller* and has a slower ascending branch, so that its peak is delayed (Fig. 9-9B).

The *aneurysm of the innominate trunk* causes *a smaller and delayed pulse in the right arm* (Fig 9-9C), an aneurysm of the left subclavian artery is followed by similar changes in the left arm

The aneurysm of the abdominal aorta is revealed by a high and slow pulsation over the pulsating mass The *femoral* pulse is smaller and has a slower rise in *comparison* with the brachial pulse (Fig 9-9D) Two simultaneous aortograms recorded at the two opposite sides of the mass may aid in the differential diagnosis with a tumor: an aneurysm has an *expansive* pulsation, revealed by *two positive pulses*, a tumor has a transmitted pulsation, and this is revealed by a positive and a negative pulse.

Fluoroscopic examination of the patient in various positions reveals the presence of pulsations of the vascular tumor. However, pulsations may be minimal or absent if the aneurysm is extremely large, the cavity is occupied by large thrombi, or the communication between the aorta and the aneurysm is narrow. The latter two circumstances also limit the value of *angiocardiography* in differentiating aneurysms from other mediastinal tumors.

ANEURYSMS OF THE SINUSES OF VALSALVA

Incidence. Of 43 proved cases culled from the literature up to 1949 by Jones and Langley, 17 were due to syphilis. Steinberg et al., with the aid of angiocardiographic examination of 2,500 patients, found 19 cases of unruptured aneurysm of the sinuses. There were 9 due to acquired syphilis; of these, 6 were associated with aneurysms of the ascending aorta, and 3 were confined to the sinuses. Other etiologic factors are congenital anomalies and bacterial endocarditis with mycotic aneurysm.

Pathology. One or more sinuses may show saccular dilatation Aneurysms of the ascending aorta, aortic insufficiency, and coronary ostia stenosis are frequent concomitant lesions In contrast with thinner-walled congenital aneurysms, those due to syphilis are larger, laminated, and less prone to perforate. Rupture may be extracardiac.

Clinical Features. Symptoms from sinus aneurysms per se are usually absent prior to perforation or rupture. When present, they arise from pressure on adjacent heart structures, particularly the pulmonary artery or conus, and on the right atrium and ventricle, resulting in the clinical syndrome of *cor pulmonale.*

Roentgen Examination. Ordinary PA conventional views do not reveal localized saccular aneurysms of the sinuses. However, they may be evidenced by the presence of calcium extending down to the sinuses from an aneurysm of the ascending aorta. *Angiocardiograms* of the LAO projection reveal the dilatations above the valves. Occasionally, a sinus aneurysm may expand posteriorly, displacing the left atrium and the esophagus and producing the radiologic findings of an enlarged left atrium.

Rupture of Aneurysms. Approximately one-half of syphilitic thoracic aortic aneurysms rupture into adjacent structures. Occasionally, rupture occurs through the anterior chest wall. The structures most frequently perforated are the pericardial sac, the left pleural cavity, the left main bronchus, the trachea, and the esophagus; less frequently, the right pleural cavity, the right bronchus, the superior vena cava, the pulmonary artery, and the right atrium or ventricle Death may occur immediately from *tamponade* of the heart, from exsanguination, or from overloading of the pulmonary vascular or systemic venous systems. Small erosions may reseal by thrombus formation, and repeated hemorrhages may ensue over a rela-

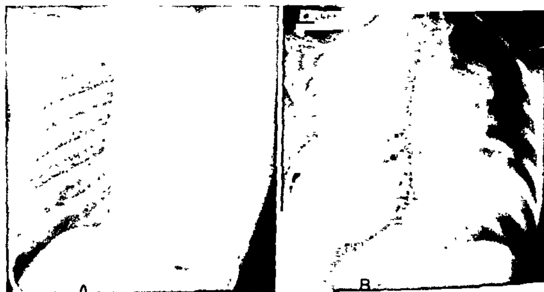


Fig. 9-8. A. Atelectasis and pneumonitis of the left lung in a Negress secondary to bronchus stenosis due to aneurysm compression. B One month later when pneumonitis had subsided.

ELECTROKYMOGRAM

Two types of tracings can be taken, border tracings and densograms of the pulsating mass.

A border tracing presents a typical pattern; the waves are large and have a slow rise and a slow fall in any case where the pouch is *expanding and contains fluid blood.* On the contrary, the pattern is identical to that of the aortic pulse when the pouch is full of clots. This tracing cannot be used for differential diagnosis with tumors because both an aneurysm and a *tumor may present border* pulsations of the arterial type because of mechanical transmission of the aortic pulse.

The densogram of an aneurysm has a large pulsation with a slow curve of the pulse. This can be easily differentiated from the densogram of a tumor which, having a poor blood supply, presents a small pulsation, or none at all (Fig. 9-10). When a tumor is over the aorta or the pulmonary artery, the most suitable projection should be selected in order *not to record the pulsation of these vessels.* Unfortunately, superimposition of vessels is very common.

In aneurysm of the pulmonary artery, typical changes are observed, not only over the *main trunk but usually also over one or both* stems. Thus, the hilar shadows frequently present large and slow pulse waves with the pattern found in aneurysms.

T-wave and S-T–segment changes in the limb and chest leads. Three had inverted T waves in lead I. In their opinion, the deviations were not due to therapy, but represent heart muscle involvement. Autopsy verification was not available.

With *aortic insufficiency,* the deformities are those of *left ventricular strain* or *hypertrophy.* Occasionally, coronary ostia stenosis is associated with patterns of *myocardial ischemia* or *infarction.* Conduction disturbances are infrequent, as are also arrhythmias, unless nonsyphilitic cardiovascular lesions are also present.

Aneurysmal compression of the pulmonary artery, with resultant *chronic cor pulmonale,* produces electrocardiographic evidence of *right heart strain* Deviations ascribed to *acute cor pulmonale* may follow rupture into the pulmonary artery or into the right heart chambers. *Paroxysmal atrial tachycardia* or *fibrillation* may develop after rupture of an aneurysm into the right atrium.

PROGNOSIS

The prognosis of cardiovascular syphilis is influenced by several factors Of major importance are the type, location, degree, and rate of progression of pathologic alterations and their effect on the function of the heart and adjacent structures Other factors include the phase of the disease when antisyphilitic therapy is instituted, the patient's race, sex, age, occupation, and the coexistence of other nonsyphilitic disease of the cardiovascular system. Life expectancy differs with each of the four major late complications of syphilitic aortitis and is further (usually unfavorably) altered by the presence of such multiple lesions.

The outlook for patients with nonaneurysmal aortic dilatation is, on the whole, good. The majority of those who are asymptomatic at the time of diagnosis and who then are adequately treated live as long as comparable nonsyphilitic individuals in the general population Patients symptomatic when first seen, and with more pronounced aortic dilatation, are relatively less fortunate

When collateral coronary circulation keeps pace with the degree of coronary ostia stenosis, and in the absence of other causes of left ventricular hypertrophy, patients may continue a productive life and unimpaired activity for prolonged periods. Life expectancy becomes considerably reduced, however, with the onset of precordial pain and when other manifestations of impaired coronary circulation appear. The absence of other complications of syphilitic aortitis does not alter the unfavorable clinical course. Nevertheless, 28 per cent of Webster's group with precordial pain survived for 10 years. *Sudden death* is common. Myocardial infarction is rare.

The prognosis, in the presence of syphilitic aortic insufficiency, depends upon the patency of the coronary orifices, the degree of regurgitation which reduces coronary flow, and the presence of other diseases which interfere with myocardial function. The state of the coronary circulation is the major factor. The asymptomatic phase may extend up to 10 years or more. Following the onset of symptoms of heart failure, the outlook is distinctly less favorable. Formerly, it was generally stated that death usually occurred within 2 years More recently, with improved methods of treating congestive failure, patients have survived up to 14 years Of 163 cases studied by Kampmeier and Coombs, 50 per cent lived for an average of 12 years from the onset of symptoms. Longevity is greater in those with sedentary occupations.

After the onset of symptoms due to compression by an aneurysm of neighboring structures, the average survival time is usually measured in months. Longevity is shortened when there is associated aortic insufficiency and coronary ostia stenosis Aneurysms of the descending thoracic and abdominal aorta may attain great dimensions before symptoms appear Specific therapy is usually ineffective in arresting the progress or in retarding the onset of symptoms. Occasionally, there is spontaneous arrest Rupture is the major hazard

Syphilitic heart disease is more rapidly progressive in Negroes and in patients who first develop symptoms before the age of 60

TREATMENT OF CARDIOVASCULAR SYPHILIS

Specific Antisyphilitic. Prior to 1943, it was reasonably established that adequate heavy-metal treatment of early syphilis afforded partial, if not total, protection against the development of late cardiovascular syphilitic lesions. In 1937, Kemp and Cochems reported

PART 10

Coronary heart disease

The former noncurative procedures, such as *wiring, electrothermic coagulation,* and *wrapping,* have been discarded. The procedures now employed are *excision of the aneurysm* and either *suturing* of the aortic wall or *replacement* of the excised segment with a freeze-dried homograft. A saccular aneurysm of the thoracic aorta with a relatively small neck may be tagentially resected and the adjacent uninvolved aortic wall sutured. Fusiform aneurysms at the proximal portion of the large branches of the aortic arch have been excised. The major hazard in aortic resection arises from the necessity of interrupting the blood supply to vital structures, such as the kidneys and the spinal cord. Employment of *hypothermia* to reduce tissue oxygen requirement and of various methods to maintain uninterrupted blood supply through a bypass has reduced the hazards. *Bilateral lumbar sympathectomy* and the injection of *heparin* into the aneurysm prior to occlusion of the distal aorta serve to reduce the impairment of blood flow and the possibility of thrombosis of the distal arteries.

The indications for surgical intervention are uncontrollable pain and increasing size of the aneurysm. Since death is not always immediate following rupture of an abdominal aortic aneurysm, emergency surgical intervention may be lifesaving. A difficult problem for the clinician is the selection for surgery of the asymptomatic aneurysm which will subsequently rupture Aneurysms with a thin wall and large lumen as revealed by aortography are more likely to rupture than those with a thick, laminated clot. Wright et al. feel that it is more logical to prevent rupture, even in asymptomatic cases, by resection and homograft.

PART 10

Coronary heart disease

A

B

C

D

Fig. 9-9. Scheme of pulse tracings in aortic aneurysms. A. Aneurysm of ascending aorta: the right radial pulse is smaller than the left; the femoral pulse is large. B. Aneurysm of the arch. the left radial pulse is smaller and slower than the right, the femoral pulse is large. C. Aneurysm of the innominate artery, the right radial pulse is smaller than the left D Aneurysm of the abdominal aorta From above: radial pulse (large); femoral pulse (small); pulse of the mass (large and slow).

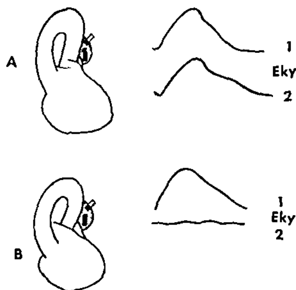


Fig. 9-10. Electrokymograms of a mass revealing expansive pulsation (aneurysm) in (A); transmitted pulsation (tumor) in (B) (1) border tracing; (2) densogram.

PHONOCARDIOGRAM. PHONOARTERIOGRAM

Various changes, caused by myocardial damage or aortic valvular lesion may be observed

Records taken over the pulsating aneurysm (ascending aorta or aortic arch) reveal a systolic and frequently also a diastolic murmur. It is difficult to say whether these are caused by the blood moving in and out of the pouch or are transmitted from the aortic valve In such a case, dilatation of the ascending aorta (relative stenosis of the ostium) would cause the first, valvular lesion (aortic insufficiency), the second

In aneurysm of the abdominal aorta, a tracing recorded over the pouch usually reveals a rough systolic murmur, seldom also a diastolic murmur.

1

Psychic factors in coronary heart disease

PHILIPPE V. CARDON, JR.

Preliminary considerations of psychic factors in structural disease are similar to those which will be presented in the chapter on psychic factors in hypertensive heart disease.[1]

CORONARY ATHEROSCLEROSIS

The possibility that psychic factors play a role in the pathogenesis of atherosclerosis is often raised but has not been sufficiently investigated. The limited information bearing on the question is of several types, each of which will be considered.

Epidemiologic considerations have led to the suggestion that the relatively high age-adjusted incidence of coronary heart disease in Western Europe, the United States, and Canada is due to the "stress" of living in these areas. As subsequent discussion will suggest, such a postulate must be taken seriously, even though diets high in animal fats are probably a major etiologic factor, and might at first seem an adequate alternative explanation. It is hard to make reliable estimates of the kinds, severity, and frequency of "stresses" in various cultures, let alone weigh their importance relative to each other and to such factors as heredity and diet. Perhaps the most one can hope for from cross-cultural studies is to gather hints as to which directions more controllable research should take. For example, Western culture is probably outstanding in the number of decisions demanded of its members. Technology has greatly increased the number and variety of stimuli, tasks, and possible courses of action which confront the individual. At the same time, the individual is encouraged to take responsibility for his own "success" or "failure." Thus one might postulate that physiologic changes conducive to atherosclerosis occur when individuals are alert, ready to evaluate a changing environment, prepared to take immediate action, and convinced that their actions will have important, though uncertain, effects on their futures.

Within our culture, some of the variations in the incidence of coronary heart disease among various occupational groups and subcultures are compatible with such a hypothesis. For example, age-adjusted coronary death rates are significantly higher in the more urbanized states in the United States, being about 50 per cent higher in the Middle Atlantic states than in the East-South Central states. It is unlikely that diet is the only factor producing such intergroup differences. The prosperous and well-fed West-North Central farming areas have a relatively low incidence. American physicians die of coronary heart disease more frequently than the average person. General practitioners, compared with specialists, are younger when they die of coronary heart disease. It can be reasonably hoped that, within the next few years, current studies designed to test such epidemiologic inferences will remove them from the realm of speculation.

[1] See Part 12, Chap. 2 Editor.

taneous" anxiety attacks which come "out of the blue" may result in sustained precordial pain at rest, with appropriate electrocardiograph T and S-T changes, which may be misinterpreted as impending or actual infarction.

MYOCARDIAL INFARCTION

Given an individual with coronary atherosclerosis, do psychic factors effect the occurrence or timing of myocardial infarction or *its immediate and long-term results?* There is often a discrepancy between the extent of atherosclerotic disease and of myocardial necrosis. Presumably, this is *in part related* to how fast coronary stenosis and occlusion occur, particularly to the presence or absence, and timing, of thrombosis It has been shown that peripheral thrombophlebitis often occurs during periods of severe psychic stress (Schneider) As to the possible mechanisms involved, abbreviation of clotting time and increase in peripheral venous hematocrit have been observed during psychic stress, whether "spontaneous" over a period of days or weeks or acutely induced over a 30-min period It is not known whether such changes, during periods of *sustained* psychic stress, persist during sleep Similar changes occur after administration of epinephrine and, in "hyperreactors," immediately after the cold pressor test Abbreviation of clotting time was observed in the *arterial* blood of cats during acute excitement (Cannon et al).

Clinically, *there is no good evidence as yet* as to whether or not myocardial infarction occurs during *acute* psychic stress with more than *chance frequency* The frequent history of *sustained* and mounting tension preceding infarction in younger men has already been *mentioned*

As to outcome, there is increasing emphasis on the role of ventricular arrhythmias in sudden deaths and of thromboembolic complications in the subacute and convalescent phases. Psychogenic arrhythmias are discussed elsewhere. The well-known observation that epinephrine predisposes to ventricular fibrillation, and the few reported examples of apparently psychogenic ventricular tachycardia occurring in patients without evidence of structural heart disease, raise the strong probability that the overwhelming fear which accompanies acute myocardial infarction can be lethal. The same sort of reasoning applies to thromboembolic phenomena.

HEART FAILURE

It is common clinical experience that severe emotional crises *sometimes immediately* precede the onset or worsening of congestive failure. This is particularly *striking in some* patients with recurrent episodes of acute pulmonary edema (Part 12, Chap. 2). It has been estimated that identifiable emotional crises precede hospitalization for congestive failure in about three-quarters of consecutive hospital admissions (Chambers et al). This surprisingly high estimate is based on information gained by an attending internist *through interviews* with patients during the first 3 days of hospitalization, at a time when they were severely ill. Such circumstances probably made it easier than usual *to elicit* important personal information. On the other hand, one must bear in mind the common human need to blame others for our troubles. Furthermore, it is reasonable to suggest that a decreasing cardiac reserve can precipitate crises in interpersonal relationships by rendering the patient unable, or unwilling, to behave as usual.

Changes in behavior may be of significance in the genesis of congestive failure. Many cardiac patients *seem to refuse to admit that they* are sick In threatening situations, the primitive need to feel invulnerable may lead to excessive physical activity and to a "forgetting" of diet and medications In other patients, the unconscious need to "spite" a frustrating environment, or to regain love, by becoming sick (a transparent device of children) may have similar results.

There are several known psychosomatic phenomena which may be pertinent, although few have as yet been proved actually to precipitate or worsen congestive failure. *Emotionally triggered supraventricular tachycardias* certainly can do so. That harm *may come* from sustained *neurogenic sinus tachycardia* or *increased blood pressure* is likely but less certain As already stated, *exercise* tolerance, judged by heart-rate responses, is often adversely affected by psychic factors.

Water and electrolyte excretion is affected by psychic factors Clinically, in all of a small experimental group of individuals with normal

may be no more accurate than his life-long dietary misconceptions.

It is well to form a clear notion of how the patient reacts to leisure as well as to work before advising a revision of the balance between them Patients' wives can be of tremendous help in this respect, or worse than useless In either event, they must be questioned cautiously. Only those wives who can carry it should share the load of planning for their husband's futures.

Serial determinations of blood lipids, begun preferably in the years preceding illness and deliberately made at such varied times as the ends of vacations or periods of difficult work, will provide at least some objective basis for judgment. Finally, consultation on this specific point with a humane and experienced older physician should always be considered.

A last note of caution is in order. Psychosomatic concepts are a contradiction of the adage that "Sticks and stones can break my bones but names will never hurt me" In his search for understanding, a physician can intensify in the immediate family the feelings of guilt which are always aroused by the illness of a loved one. He and his patient must be alert to this complication It is a physician's duty to learn the truth when the learning will do no harm. It is vastly more difficult —and rewarding—for the physician to use his knowledge wisely

Individuals who have had myocardial infarction have been studied from the psychologic point of view. It has been claimed that, as a group, they are outstanding in being hard-working, aggressive men who attain positions of authority, play the role of exemplary husband and father, carry more than their share of the family burden but demand care and attention in return, live for the future, and brood and keep troubles to themselves, rarely admitting their depression and inner tension to others (Dunbar).

Subsequent better-controlled studies have differed in the success with which they detect psychologic differences between patients with coronary disease and controls. One study found that the similarities between men with a history of coronary occlusion before their forty-first birthdays and healthy controls were more striking than the differences, but found that the former tended to work harder under more strain, were less reflective, and expressed aggression more readily (Miles et al.). On the other hand, in a comparison of hospitalized coronary patients with control patients of similar age, striking differences were reported (Weiss et al.) Briefly stated, the findings were that each of various indices of long-standing emotional maladjustment was present in roughly one-third to one-half of the coronary group, but in only one-half as many of the controls Of particular interest is the history of "gradually mounting tension" in the months or years prior to occlusion in two-thirds of the coronary patients under 60, and in only one-fourth of those over 60.

If psychic factors are important in the genesis of atherosclerosis, how do they operate? *Nervous overeating and smoking are obvious possible mechanisms* There is surprisingly little information on the more direct effect of psychic factors on blood lipids In studies done more than 20 years ago, it was shown that *acute excitement in cats and rabbits can increase blood cholesterol* (Lyons; Katz et al.) To the author's knowledge, these findings have subsequently been neither confirmed nor contradicted. Apparently, the sympathoadrenal system is important in the mechanism of these acute rises. More recent animal work confirms the observation that, depending on the dose and route of administration, *epinephrine may increase all major lipid fractions*

Published reports of the effects of various "stresses" on blood lipids in humans are few but auspicious. Most of the information, though still fragmentary, is on cholesterol. Within minutes or hours, it is said to rise moderately during acute anxiety or immersion in cold water. Conversely, it falls slightly but significantly after an hour's "quieting" under hypnosis. In the first week or two of acute infections, x-ray treatment, sustained psychic stress, and postoperatively, it falls below prestress levels and in subsequent weeks often rises above prestress levels. In a minority of individuals on constant fat diets, marked fluctuations of blood lipids occur. It is the impression of some investigators that such fluctuations are related to periods of sustained tension and worry. The practicing physician has a unique opportunity to make observations in this area.

PRECORDIAL PAIN

That the pain of myocardial hypoxia may be precipitated, in patients with coronary heart disease, by a variety of emotional experiences is a clinical truism. The mechanism is probably that of increased cardiac work and myocardial oxygen requirement, as during exercise. The weight of evidence is against neurogenic coronary vasospasm as an alternative mechanism It is perhaps less well appreciated that the exercise tolerance of patients with coronary disease, in fact that of most people, varies according to their moods (Stevenson et al.).

Although a careful history can usually make the distinction, noncardiac chest pain and tenderness are frequent but still mysterious symptoms in "nervous" people. Such pain is often aggravated by exercise. Knowing that he has heart disease is apt to make a patient nervous, even though he may not show it. The presence of precordial pain of coronary origin does not preclude the possibility that many of the chest symptoms are *not* of cardiac origin. It is not sufficient to tell the patient that his chest pain comes from his heart. If, by careful evaluation, the physician concludes that some of the symptoms are noncardiac in origin, he should not only tell the patient that this is so, but try to educate the patient to distinguish in his own mind among various types of chest pains. It must be borne in mind that "spon-

branch is usually supplied by both arteries, generally from septal branches of the left anterior descending branch and small vessels from the right coronary artery. The arborization systems receive their blood from arteries supplying the myocardium.

As shown by Whitten, there are differences in the manner of branching of the coronary arteries in the two ventricles, and these are important for hemodynamic considerations. The branches of the left coronary artery are *deep penetrating* ones extending the depth of the myocardium of the left ventricle. At each point of penetration, the artery becomes more or less fixed and some buckling of the vessel can be demonstrated. The right coronary artery is a rather superficial vessel, smaller than the left, and its ramifications into the myocardium of the right ventricle are gradual rather than abrupt; furthermore, in the right ventricle, the branches are given off in the same plane in which lie the larger arteries, while in the left they turn sharply, almost at right angles, at the point of penetration into the myocardium.

In about 8 per cent of persons, the orifice of the right coronary artery is located in the wall of the aorta above its normal position in the cusp. In this abnormal location, it is more likely to be occluded by an arteriosclerotic or syphilitic plaque.

A *single coronary artery* may adequately supply the whole heart without damage to the myocardium. However, studies of such cases have shown that the right coronary artery alone is less able to maintain an adequate blood supply than the left alone. Either or both coronary arteries may also arise from the pulmonary trunk.

In the average normal heart then, the blood supply to the heart conforms to the following pattern:

Left coronary artery
- Entire anterior surface of the left ventricle
- Adjacent one-third of the right ventricle
- Apex of both ventricles
- Anterior two-thirds of the interventricular septum
- All of the apical part of the septum
- Left half of the posterior left ventricle
- Left atrium

Right coronary artery
- Two-thirds of the anterior right ventricle (except the apex)
- All of the posterior surface of the right ventricle (except the apex)
- Posterior one-third of the interventricular septum (except the apex)
- Basal three-fifths of the posterior surface of the left ventricle
- Right atrium

However, this general distribution pattern is far from being constant. Three distinct patterns of distribution have been shown.

Right Coronary Predominance. In a series of 225 adult hearts, 48 per cent were of this type; in them, the right coronary supplied all the right ventricle, the posterior half of the interventricular septum, and a large part of the posterior wall of the left ventricle.

A Balanced Circulation. There were 34 per cent of hearts of this type, and they generally followed the distribution shown for the average normal heart.

Left Coronary Predominance. In this group, there were 18 per cent. In them, the left coronary artery supplied all the left ventricle and the entire septum; in some cases, it also supplied a part of the right ventricle (over its posterior surface) and, anteriorly, the region around the pulmonary conus, as well as the right ventricular side near the left anterior descending branch.

The capillary and venous channels are important in so far as they contribute to the formation of anastomotic channels. The myocardium contains an extensive web of *capillaries* which course among the cardiac muscle fibers. These capillaries are fed by branches of the various coronary arteries and are drained in part by the coronary veins. Injection studies have shown that there are, in addition, *anastomosing vessels* which connect adjacent branches of the same coronary artery, branches of the right and left coronary arteries, the coronary arteries and veins, and branches of the coronary veins. About 9 per cent of hearts contain extensive anastomotic channels at birth; in the remainder, these anastomoses are small and some of them may be absent. If there is a sudden occlusion in this group, the coronary arteries may behave as *terminal* arteries. In many instances, however, the anastomoses are capable of gradual enlargement and may be found to be functionally significant.

The intramyocardial vessels possess another peculiarity. Channels pass from the arterioles, capillary bed, and coronary veins directly into the lumen of the cardiac chambers. Such venous channels are known as the *thebesian veins*, and the arterial ones as the *arterioluminal vessels*. The latter may empty either at the surface of the trabeculae or, as is more usual, into the intertrabecular spaces. They might be considered as *venae minimae cordis* since they possess the histologic characteristics first of an arteriole and then of a muscular artery at variable depths within the myocardium. Deep within the myocardial musculature, there also is a richly anastomosing network of thin-walled irregular channels called *myocardial sinusoids*. These receive vessels from both

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during childhood and again during adolescence. Some of these *undoubtedly retrogress, leaving* either a grossly normal intima or minute *fibrous* plaques devoid of lipids

pattern of the reactive changes *characteristic of that location.*

With advancing years, the intima develops *nodular thickenings*, first at points of bifurcation and later along continuous areas of artery Within such nodules, foci of lipid and calcium deposition appear at the base; except for the small crops of lipid deposition in infancy and adolescence *noted* above, these are late developments. Elastic fibers degenerate, fragment, and *calcify both* in the *intima* and media, and new elastic *elements form* concomitantly. Intima and media eventually fuse, smooth muscle fibers atrophy, and irregular patches of connective *tissue appear in* the media

Vascularization of the arterial wall develops as it thickens. *As* Winternitz and Le Compte have *shown*, this takes *place in part* by arborization of branches of the vasa vasorum through the media and *in* part *by the* development of capillaries in the intima which communicate with the lumen through stomata of the endothelium; the two combine to form



Fig. 10-1. Various stages in *the* process of plaque *formation in* coronary arteries. The black-on-white *illustrations* are of elastic tissue stains, *the white-on-black* are of microincinerated specimens. A, B An infant's coronary artery, showing the internal elastic membrane as a single band just beneath the *inner* lining, and only a thin line *of calcium* on incineration C. Early fraying and reduplication of elastic tissue, with *corresponding* calcification *shown* in D. E. Progression of fraying and reduplication of elastic elements as *the intima* progressively thickens.

hearts, wide variations in water and electrolyte excretion, independent within broad limits of intake, have been closely correlated with various feeling states, which in turn were responses to changes in the environment (Schottstaedt et al.). Retention of water and sodium usually occurred during periods of "tension" (that is, in situations which involved sustained alert performance, but which were not frightening) and at times of hopelessness and exhaustion. Sodium and water diuresis occurred at times of release from tension or lifting of depression and during overt fear or anxiety. Most individuals can confirm from personal experience that fear often is accompanied by *polyuria*, but this is apparently not always so. Actually, a marked *suppression of urine output* has been observed during extreme fright.

The mechanisms of these changes are not well understood and are certainly complex. The antidiuretic hormone is secreted by hypothalamic neural tissues. Diuresis induced by water loading, in animals and human beings, can be completely inhibited by painful stimuli, presumably through release of ADH Secretion of aldosterone, the sodium-retaining adrenal-cortical hormone, is increased in congestive failure. As its secretion appears to be under hypothalamic control, it is almost certainly subject to psychic influences. Sympathetic and adrenal-medullary activity, through complex effects on the renal circulation and the central nervous system, can cause either diuresis or antidiuresis.

Finally, prolonged sitting can cause dependent edema even in normal individuals. The symptom of lassitude is common to both congestive failure and psychic depression, as is the age group in which these syndromes are most likely to occur. Cardiac patients may sit because they are afraid to move or, more frequently, because their bleak world holds no incentives to be up and doing

THERAPEUTIC CONSIDERATIONS

The foregoing discussion has been concerned mainly with the possibility that psychic factors may affect both the genesis and the course of coronary heart disease If more solid affirmative evidence accumulates, the greatest therapeutic challenge will lie in the areas of public health, "mental hygiene," and social values. Whether affirmative or negative, further evidence need have relatively little effect on the conduct of the individual physician The certainty that his sensitivity and compassion are an important part of treatment needs no scientific underpinning.

Coronary heart disease raises a particular kind of psychic problem. Though he may feel perfectly healthy, the patient knows he may die suddenly. Once the diagnosis is made, no amount of reassurance can abolish his fear. Both physician and patient may push this fear into the backs of their minds, tacitly agreeing that it does not exist, but the treatment prescribed, the continuing follow-up, and the death of others will inevitably revive it. The physician performs a real service if he can deal openly with this fear and help the patient to reduce it to manageable proportions. The physician does this best when he has made a satisfying adjustment to his own mortality

A working knowledge of the manifestations and treatment of psychic depression is of great importance. The reader is urged to foster his skills in this area through any facilities which may be available

When dealing with a disease as unpredictable as coronary heart disease, the physician must cover some of his uncertainties with the mask of confidence The patient needs a list of things which he should and should not do. Obviously the list will be different for each patient It should be clear from the start as to which prohibitions are absolute, which tentative, and why One must be alert to the patient's and his family's preconceptions as to what the list should contain. Any hint of discordance should be pursued vigorously until understanding is reached *This is doubly important if, in preference to "playing it safe," the physician chooses thoughtfully to balance the risks of the disease as such against the risks of unnecessary invalidism.*

Advice about occupation is crucial and difficult Decisions as to permissible physical effort present problems which cannot be gone into here. One hesitates to propose any rule of thumb as to how "tough" a job a patient with coronary heart disease should attempt. *A man's feelings that a job is too much for him must be given weight and respect without moral judgment* On the other hand, his conviction that he "thrives" on his current job

circumflex shows thrombosis in only about 6 per cent. Yater et al. have shown a similar distribution for complete or almost complete sclerotic occlusion. Again, it is usually in the proximal one-third of the vessel that these phenomena occur.

Medial calcification of muscular arteries, as described by Monckeberg, is also seen in the coronary circulation but, as a rule, is not so severe as in the arteries of the lower extremities. Perhaps this is because the hemodynamic transition from stem to branch is more abrupt in the coronary system than in other locations, or possibly because of a difference in the response of coronary arteries to norepinephrine. Such calcific changes have also been observed in the arteries of infants, where they have usually been attributed to some type of metabolic disturbance.

Odel has shown that *hyaline and hyperplastic sclerosis occur in intramyocardial branches just as in comparable sized channels in other organs in hypertensive states.* Saphir et al. reported such changes in 82 of 100 hearts from patients less than 50 years of age with advanced sclerosis of the extramural coronaries; the significance of these observations is discussed below.

Inflammatory Coronary Artery Disease. Inflammatory diseases of the coronary arteries fall into several groups, i.e., infectious, allergic, toxic, and those of unknown etiology. Gregg estimates that the last group plus certain congenital lesions make up only about 5

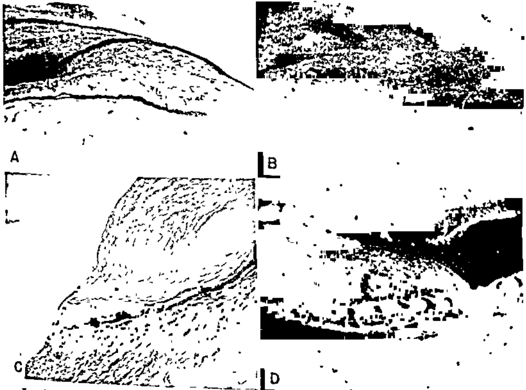


Fig 10-2 A Advanced plaque formation in coronary arteries with a concentration of filamentous elastic elements, the calcification of which is shown in (B). This process progresses to the replacement of elastic elements by collagen and the appearance of lipids at the base of the plaque, as shown in (C), elastic filaments are present only at the junction with the intima, and a thick elastic membrane is formed at the base of the plaque. Filamentous elastic elements are also present through the media. Calcification is present through the media, at the base of the plaque, and at the junction with the intima, it is largely absent in the bulk of the plaque, as shown (D), which is a mirror image of (C)

2

Pathology of coronary heart disease

HERMAN T. BLUMENTHAL

The heart, as any other organ, has a critical dependency upon its blood supply. A discussion of the pathologic changes in coronary heart disease, therefore, includes two broad areas: (1) the pathologic changes in the coronary arteries and (2) the effect of impaired coronary function on the various structural components of the heart. The anatomic distribution of the coronary system and its variations determine the localization of cardiac injury. Since the circulation to the heart is not a static system, factors influencing the development of collateral circulation should also be considered.

ANATOMIC CONSIDERATIONS [1]

Gross Anatomy of the Coronary Circulation. Two coronary arteries, the right and left, carry blood to the myocardium. The *left coronary artery* arises from the aorta opposite the left posterior sinus of Valsalva, runs forward over the anterior surface of the heart between the pulmonary artery and the left atrium, and about 2 mm from its origin divides into the left circumflex and the anterior descending branch. The *left circumflex* swings around the base of the left atrium in the coronary sulcus, to reach the diaphragmatic surface of the heart where it ends as the *left posterior descending* branch, coursing over the posterior aspect of the left ventricle. Along its route, the left circumflex sends off many small arteries to supply the root of the aorta, left atrium, and left ventricular wall. To the left of the posterior longitudinal sulcus, adjacent to the coronary sinus, the circumflex branch anastomoses with small arteries from the right coronary artery. The *left anterior descending branch* runs downward toward the apex in the interventricular groove; in its course, it sends *perforating rami* into the substance of the interventricular septum, to supply the anterior part of the latter, and into the adjacent ventricular myocardium. It generally extends around the apex posteriorly, supplying the posterior apical portion of both ventricles.

The *right coronary artery* arises near the upper border of the anterior sinus of Valsalva. It passes downward and to the right in the coronary sulcus to reach the posterior longitudinal sulcus. Here it divides into a large *right posterior descending branch*, which continues along the length of the posterior longitudinal sulcus, and a smaller branch, which anastomoses with the circumflex branch of the left coronary artery. The first branch of the right coronary artery passes into the musculature of the pulmonary conus in about one-half of adult hearts; in the other half, an independent artery arises from the right sinus of Valsalva. The right coronary also gives off fairly large branches, the *right marginal artery*, which extends downward along the right margin to the apex, and the *preventricular branches*, which supply the anterior surface of the right ventricle. It also gives off smaller branches to supply the root of the aorta, the initial part of the pulmonary trunk, and the right atrium. The *right posterior descending branch* gives off *perforating rami* to supply the muscle of the posterior part of the interventricular septum and the adjacent posterior right ventricular wall.

The *SA node* is supplied by a branch of the right coronary artery, originating near its ostium in about 70 per cent of human hearts; in about 25 per cent, it is supplied by a branch of the left coronary, and in 7 per cent from both vessels. The *AV node* is supplied by the right coronary artery in about 92 per cent of hearts. The *right bundle branch* generally obtains its blood supply from the anterior descending branch of the left coronary artery, but may be supplied by both right and left coronary arteries. The *left bundle*

[1] See Part 1, Chap. 7. *Editor.*

also appear *to* develop predominantly in younger age groups.

The approach utilized by Saphir et al. *to* determine *those cases* of coronary arteriosclerosis which may be on an inflammatory *basis* appears worthy of consideration. It is based *on the thesis* that all segments of the coronary artery system are equally involved (*in contrast* to the most common form of arteriosclerosis), *but that the* lesions of the large extramural arteries in late stages are indistinguishable *from* lesions having a different etiologic basis. He *has therefore* made a careful study of the small *intramural* arteries for evidence of inflammatory disease, he considers among the latter intimal proliferation, fibrosis of media and adventitia, and hyalinization, *with or* without perivascular infiltrates. Analysis of autopsy findings and clinical histories disclosed that *hypertension was present* in 23 of the 82 patients, diabetes in 7, a clinical history suggestive of hypertension in 12, evidence of recurrent old endocarditis in 10, and a history *of rheumatic* fever in 2. Of the remaining 33 cases, 10 disclosed glomerulonephritis or nephrosis and 5 showed chronic infectious diseases. *In the remaining* 18 *cases*, where there was no apparent etiology, at least 6 showed microscopic changes which could be explained on a *hypersensitivity* basis. The possibility is *raised* that such hypersensitivity states might be related to the common use of antibiotics and chemotherapeutic agents.

The foregoing observations suggest that there is strong evidence that an inflammatory basis for coronary arteriosclerosis may be considerably more frequent than is generally realized. This appears to be particularly applicable to cases under 50 years of age. Whether such inflammatory lesions uniformly involve all segments of the coronary circulation or only the intramyocardial portions remains in doubt. Nevertheless, severe involvement of the intramural channels may produce a peripheral resistance which might secondarily involve the larger coronary segments on a hemodynamic basis. Furthermore, the inflammatory obliteration of numerous small intramyocardial rami may preclude the development of collateral channels in the event of marked narrowing of the major branches.

Metabolic Coronary Artery Disease. In recent years, lipid metabolic factors, particularly those have [illegible] ology of coronary arteriosclerosis. Data to [illegible] port this concept fall essentially *into* the *following categories*:

1. The presence of cholesterol and other lipids in atheromatous plaques in concentra*tions similar* to those found in the circulating blood

2. The experimental production of athero*sclerosis* by the *elevation of* plasma lipids, including cholesterol

3. The increased incidence of atherosclerosis *in various* clinical states *of hypercholesterolemia* and *hyperlipemia*

4. The finding of quantitative, and *possibly qualitative*, differences from normal of plasma lipid transport in *atherosclerotic individuals*

5. A seemingly close relationship between intake of dietary lipids, including cholesterol, and the incidence of atherosclerosis in various population groups

A critical evaluation of the validity of the data in each of these categories as regards the human disease has been dealt with in detail by Friedman et al. and by the author.

As *regards the* presence of various lipids in atheromatous lesions, the basic question which remains to be answered *is whether these* substances first appear in the lesion and initiate the appearance of the other components of the intimal plaque *or represent only a by-product* of *local degenerative* changes in the development of the latter. Primary lipid deposition does occur in the crops of *small plaques in infancy and adolescence, but many of these* regress. On the *other* hand, the investigations of *Rinehart et al.*, Levene, and the author sup*port the view that in the* large majority of plaques the *lipids* appear late, and in the depths of *the lesions rather* than on the surface, *where they would* be *expected* on the basis *of infiltration from* the circulating blood.

The *experimental production of atherosclerosis*[3] *is subject to two basic criticisms.* In *the first place, the levels of hyperlipemia are considerably greater than those generally found in human diseases. Secondly, the* [illegible] *of the experimental lesion is* [illegible] *As regards the latter in the* [illegible] *the investigations of* [illegible]

[3] *See Part* [illegible]

the coronary arteries and capillaries and communicate with the coronary veins.

In general, capillary counts are considerably higher in the ventricles than in the atria or in the conducting system At birth, there are five to six muscle fibers to each capillary. As the muscle fibers increase in size, the fiber-capillary ratio decreases progressively to approximately one capillary per muscle fiber. Throughout the growth period, the concentration of capillaries per unit area remains essentially constant, thus, the increase in muscle mass appears to be accompanied by an increase in total number of capillaries. After full growth, the normal hearts of adults maintain an approximately constant capillary concentration and the muscle fibers remain at the same size, so that the fiber-capillary ratio is maintained.

Microscopic Anatomy of the Coronary Circulation. The coronary arteries may be considered arteries of the fourth order since their caliber corresponds to that of the distal portion of the radial arteries They are essentially of muscular type, showing a sudden transition from the elastic aorta.

The coronaries, as well as other arteries, are not static structures, but show a *continuing pattern of change* Two interpretations may be placed upon these developmental alterations which progress with advancing years; (1) they represent processes of development and growth, or (2) they are essentially responses of vascular tissue components to hemodynamic forces A basic objection to the first is that there is no distinct period at which growth levels off and degenerative phenomena set in. In this regard, Lober states that "there is no point at which the artery can be said to have stopped growing or developing and started to degenerate or become diseased" Rather, it appears that certain basic degenerative and reparative reactions occur continuously throughout life, probably in response to hemodynamic forces. The latter may even act in the embryo as determinants which influence the initial structural characteristics of a given artery since the latter appears to be able to cope most advantageously with the magnitude of the hemodynamic forces which occur at the anatomic site at which it must function While, in general, there appears to be a more or less direct *correlation with age*, and these processes may thus be considered an aging phenomenon, they can be considerably intensified by hemodynamic influences.

The author's studies, as well as those of Schornagel, have shown that at birth there is no definitive intimal layer over most of the arterial circulation; the endothelium appears to rest directly on the internal elastic lamella, which in turn lies on the innermost layer of medial muscle. However, even in the newborn, fibroelastic intimal cushions are occasionally seen, usually at points of branching According to Moon and Rinehart, the earliest changes in the development of the intima consist of the appearance of subendothelial deposits of mucopolysaccharide followed by a splitting or reduplication of the internal elastic lamella There follows an appearance of mesenchymal cells, new formation of elastic fibrils, and an ingrowth of muscle fibers. According to Schornagel, many of these changes develop relatively rapidly during the first year of life; the fibroelastic intima may become as thick locally as the media during this period.

Dock believes that, on the average, the coronary arteries of newborn males are approximately three times as thick as those of newborn females. This idea has been supported by Fangman and Hellwig who believe that this difference is not inherited but rather represents the earliest stages of arteriosclerosis. Lober and Minkowski have been able to demonstrate this sex difference only after the first month of life, and according to Lack, the thickening occurs only at points of branching On the other hand, Schornagel has been able to find only a slight sex difference of doubtful significance.

After the fifteenth year, the intimal tissue becomes increasingly thicker, and within it, there also develops a longitudinal layer of smooth muscle. These changes are fully developed by the thirtieth year, when the organized intima is seen to consist of an inner subendothelial layer of connective tissue beneath which there is a prominent elastic-hyperplastic layer, which in turn covers a musculo-elastic layer The media is composed of circularly disposed muscle fibers which are accompanied by elastic fibrils. The latter are delicate in the inner half and coarse in the outer half of the media, but no definitive elastica externa is present. Instead, there is a continuum of the coarse elastic fibers into the collagenous and fatty tissue of the adventitia.

Fatty flecks or streaks in the intima occur

system and is not equally operative in other arterial systems, no explanation is offered for this selectivity. The temporary intensification of intimal plaque formation in males at about the time of puberty also suggests a hormonal factor, but this phenomenon is not limited to the coronary circulation. Walker et al. have noted an elevation in serum cholesterol levels with age in the female and suggest that, since this substance is a precursor of steroid hormones, a decrease in hormone production in old age may account for the relatively high cholesterol levels. Perhaps it is erroneous to use the male disease as a frame of reference in this problem since we may be dealing with a situation peculiar to the female when there is cessation of the ovarian function.

The possibility that changes in lipoprotein patterns may represent effect rather than cause appears to have been overlooked. It is possible that, in severe coronary artery disease, lipid material from plaques or from degenerating myocardial cells may be released into the blood stream and a change in lipoprotein pattern result therefrom. Wartman et al. have recently shown that, in the dog, neutral fat appears in appreciable quantity within the sarcoplasm of myocardial fibers partially injured by ischemia. Most of these fibers probably experience a reversible injury, although some eventually die after accumulating large amounts of fat.

Population studies also remain inconclusive. As Friedman et al. point out, "the possible relationship between lipid and/or cholesterol intake and the pathogenesis of atherosclerosis is beclouded by the presence of other complicating factors." The latter include the frequency of hypertension in such population groups, hereditary and familial tendencies, tobacco habits, and the incidence of emotional stress and strain.

In general, proponents of the lipid metabolic theory believe that elevated serum lipids lead to a deposition of these substances in the intima and that this process initiates plaque formation. Recent observations that lipids increase the coagulability of human plasma suggest the possibility that the initiating event may be a deposition of fibrin, with subsequent organization to form a plaque. The role of fibrin deposition as an early event has been particularly stressed by Duguid and by Levene, although they have not implicated serum lipids as a precipitating factor.

There appears, then, a clearly definable area in which lipid metabolic factors play a primary role; this includes familial hyperlipemia and hypercholesterolemia and certain other metabolic disease entities associated with a prolonged, almost continuous elevation in serum lipids. There is another considerably larger area in which the evidence for a primary role of lipid factors is at best only suggestive. On the other hand, the role of abnormal polysaccharide metabolism has hardly been explored. To attribute all or most cases of coronary artery disease to lipid metabolic factors may tend to exclude a consideration of other, at least equally important, factors.

Hemodynamic Factors of Coronary Artery Disease. An analysis of hemodynamic factors operating in the coronary circulation offers the best prospect for accounting for the distribution of intimal plaques, if not also for their pathogenesis. The effects on arteries of such factors have been considered by some as reparative reactions to "wear-and-tear" injury and by others as compensatory in character, serving to maintain hemodynamic equilibriums.

Proponents of the lipid-metabolic thesis either regard hemodynamic factors as of secondary importance in that they influence only localization of lesions or consider their effects as unrelated to plaque formation. However, hemodynamic forces and vascular responses to them are not uniform throughout the body, and it appears that a correlation can be developed between such forces and responses on the one hand and the localization and development of plaques on the other. As pointed out under anatomic considerations, serial studies on progressive phases through which intimal plaque development proceeds indicate that in the large majority of instances the lesion represents a progressive response of vascular tissue components to hemodynamic forces, in which the appearance of lipids is a late development and may represent an incidental byproduct of the reactive process. In addition, the complications of thrombosis, aneurysm formation, and rupture are best accounted for on a hemodynamic basis.

Important hemodynamic factors which deserve consideration in the development of arteriosclerosis of the coronary artery system are

a complex network through the entire thickness of the vessel wall.

A comparison of the foregoing processes in the main stems of the two coronary arteries shows that, in the left, the intimal connective tissue reactions are less and the elastic hyperplastic and elastic muscular responses better developed, while the media of the left coronary artery contains relatively more and coarser elastic fibers Furthermore, all these phenomena develop most rapidly in the largest segments of the coronary system and diminish in intensity in direct relation to the diminution in caliber of the vessel. In arteries of comparable size, they are more intense at points of branching than elsewhere

Eventually, there results a gradual diffuse distention of the coronary arteries both in a transverse and longitudinal direction, so that the vessels become *longer* as well as *wider* and assume a tortuous course As the diameter of the lumen increases, so also does the thickness of the wall. Thus, during the average life span, the cross-sectional area of arteries increases six to seven times and the number of macroscopically visible arteries is doubled. The number of vessels distributed to the pericardial fat also increases with age (Fig 10-1).

DISEASES OF THE CORONARY ARTERIES

In a review, the author introduced the concept of "response potentials of vascular tissues" in the pathogenesis of arteriosclerosis According to this concept, *arteriosclerosis is regarded as a complex mixture of degenerative and reparative processes leading to increased rigidity, diminished elasticity, and decreased caliber of arteries*[2] The characteristics of the end-stage arteriosclerotic lesion in any particular anatomic site was shown to be more dependent upon the initial structure of the artery in that location and the response capabilities of its various components (endothelium, collagen, elastic tissue, muscle, and vasa vasorum) than upon the nature of the injurious agent.

In general, etiologic agents capable of eliciting responses of vascular tissue components fall into three categories (1) inflammatory, (2) metabolic, and (3) hemodynamic As in the glomerulus of the kidney (where the end-stage lesion in a variety of disease states is complete hyalinization) or in the liver (where the final lesion is cirrhosis), the final lesion in the arterial system in any particular site may be similar, whether it develops from inflammation, the primary deposition of some metabolic substance, or as a response to hemodynamic factors.

In this section then, diseases of the coronary arteries are presented within this frame of reference. Within the coronary arterial system may be found the total spectrum of changes seen in the arterial system generally. Thus, arteriosclerosis is usually considered as a process characterized by *atheroma* formation of elastic arteries and large elastic and muscular branches. Monckeberg *sclerosis* of large muscular arteries, and *hyaline or hyperplastic sclerosis* of small arteries and arterioles, the latter showing significant development in hypertension and other disease states Furthermore, it is generally recognized that, as arteries diminish in caliber, so also does the intensity of the arteriosclerosis.

Coronary arteriosclerosis is greatest in the main stem of the left coronary artery and the left anterior descending branch and less severe in the following arteries in the order named: right main coronary, left circumflex branch, right posterior descending, and right marginal branches. As a rule, the degree of sclerosis in each of these vessels is greatest in the proximal third, less in the middle third, and least in the distal third. Atheroma formation is a prominent feature in all these major rami (Fig 10-2) In only 5 of the 120 hearts studied by Wolkoff were arteriosclerotic changes more severe in the right coronary than in the left, and in 4 of them, the left circumflex branch was poorly developed and its function largely taken over by the right coronary

A similar distribution is found as regards obstructing lesions of these vessels *Over 50 per cent of occlusions may be found within 3 cm and about 80 per cent within 6 cm of the coronary ostia* In about two-thirds of the cases of coronary thrombosis, the obstruction is found either in the left main coronary artery or in the left anterior descending branch, usually in the latter Thrombosis of the right coronary occurs in about 20 per cent of cases, that of both coronaries in about 8 per cent; the left

[2] See also Part 15, Chaps. 1 to 4 *Editor*

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to 10 per cent of all so-called nonatheromatous coronary lesions. This is in contrast to the findings of Saphir et al. previously noted.

Infectious diseases which may involve the coronary arteries are syphilis, tuberculosis, brucellosis, typhus, typhoid, subacute bacterial endocarditis, and possibly, rheumatic fever. The suggestion that coronary artery disease might be infectious probably stems from the discovery of syphilis as a cause of chronic obliterative endarteritis. In approximately one-third of patients with syphilitic mesaortitis, the orifice of one or both coronary arteries is reduced in caliber. The ostium of a coronary artery is more likely to be so involved if it is anomalously located above the sinus of Valsalva, inasmuch as the syphilitic lesion usually stops at the upper level of the sinus Syphilitic coronary arteritis is not limited to the portion of the artery included in the wall of the aorta, but may extend for 10 to 12 mm beyond the orifice to produce stenosis or occlusion of the lumen. Only rarely does syphilitic narrowing of the coronaries lead to myocardial infarction, presumably because closure is so gradual that collateral circulation can develop Syphilitic aneurysm of a coronary with thrombosis has also been reported, and Martland has observed rupture of such an aneurysm.

In most instances of *infectious coronary arteritis*, the lesion probably results from a bacteremia. In subacute bacterial endocarditis, however, the lesion may be *embolic* in nature Approximately one-half of the reported cases of coronary artery embolism have been associated with this disease Such emboli consist of fragments of vegetations and usually contain bacteria as well as fragments of calcium Moragues et al have reported a case in which the embolus consisted solely of a fragment of calcium originating from a nodular calcified aortic valve without bacterial endocarditis Emboli have also been reported from intracardiac mural thrombi, from mural thrombi of arteriosclerotic or syphilitic aortas, as paradoxic emboli in cases of thrombophlebitis, and as emboli of atheromatous material from aortic plaques

Klotz was among the early investigators to associate arteriosclerotic lesions with rheumatic fever. Subsequently, Karsner and Bayless found inflammatory lesions of the coronary tree in all the 56 rheumatic hearts they studied. More recently, this disease has been discussed as an important cause of coronary arteriosclerosis in young individuals by Saphir and Gore.

As to *allergic coronary arteritis*, fatal cases have been reported following respiratory infections, antisyphilitic therapy, injections of serum, tetanus antitoxin, or typhoid vaccine, and due to drug hypersensitivity. Such fatal accidents may be caused by an acute swelling of the arterial intima (acute urticaria). It is conceivable that nonfatal cases of this type might progress to a stenosing sclerotic lesion of coronary arteries Paterson considers hypersensitivity as a possible basis for an inflammatory lesion of the coronary arteries of chicks.

Involvement of the coronary arteries in various *collagen diseases* has been observed, but frequently these involve primarily the more distal segments of the coronary circulation. Occasionally, the larger vessels may be involved in *periarteritis nodosa*. Some forms of necrotizing arteritis, as in malignant hypertension, are difficult to categorize from a pathogenetic point of view. They can be produced experimentally by a variety of substances, some hormonal, others chemical and possibly toxic. Multiple injections of various vasopressor amines may lead to a chronic form of necrotizing arteritis involving the coronaries; in a period of 6 to 8 weeks this may progress to an obliterative endarteritis. Similar lesions have been produced in dogs by Holman with a combination of renal insufficiency and a high fat diet, he notes a striking resemblance of some of the healing and healed lesions to the so-called spontaneous arteriosclerosis in dogs. In human beings, von Albertini and also Bredt have marshalled evidence for the identification of a stenosing lesion of coronary arteries with *thromboangiitis obliterans*, possibly also a toxic arteritis Bredt concluded that involvement of the coronary arteries in this disease was the underlying factor in fatal juvenile coronary arteriosclerosis in seven cases.

There remains a group of cases of inflammatory nature involving the coronary arteries which have been designated "stenosing coronary arteritis" by Zak and coworkers. These cases show a stage of necrosis with acute inflammatory reaction followed by irregular fibrous replacement of the media and segmental adventitial hyalinization. Such lesions

during systole. In this way, the coronary system is protected from the sudden ejection by the heart of a mass of blood; it may also account for the infrequency of intense plaque formation at the coronary ostia. Nevertheless, the flow of blood in the coronary system is intermittent, and the stream presents rapid changes in pressure and velocity. With the anatomic characteristics of rapid tapering in the extramural coronary arteries, reflections and eddy currents commonly occur. In addition, flow and pressure, and hence resistance, fluctuate not only with each cardiac cycle but also in response to a variety of other stimuli, including respiration.

VIBRATION. Whenever tension is suddenly changed in the arterial system, free vibrations are set up. Conditions for such vibrations are most favorable in the most proximal portion of the aorta and its branches and appear during the beginning of ejection of blood from the heart and upon closure of the semilunar valves. When the left ventricle ejects large volumes into a lax aorta, a second set of free vibrations is superimposed at the top of the initial steep rise in pressure pulse. To what extent these are transmitted along the walls of the coronary arteries is not known. Nor is it known what role such vibrations may play in the deterioration of various tissue elements in the wall. It would also be important to determine what effect increasing rigidity of segments of the coronary arteries would have upon the transmission of such vibrations. Aside from such an effect, they could conceivably play a role in the development of eddy currents.

GRAVITY EFFECT—STATIC PRESSURE. It is well known that positional changes affect the speed of blood flow. In general, the circulation time is lengthened by a position approaching the vertical and shortened by a position approaching the horizontal. The static pressure related to the vertical position is therefore a factor to be considered in the summation of all pressure effects occurring in the arteries. The effects of prolonged positional changes on the coronary arteries, specifically, is largely unknown, and the only common existing basis for comparison is between man and the four-legged animals. Whether or not position may be a factor can be conjectured only on the basis that animals seem to have a considerably lower incidence and severity of coronary arteriosclerosis than humans. Many other factors undoubtedly play a role in this difference.

Certain special conditions relating to the intrathoracic location of the heart also deserve consideration. In general, blood pressure recordings indicate the effective distending force on vessels when the surrounding tissue pressure is equal to that of atmospheric pressure. In the thorax, the distending pressure is greater because the surrounding tissue pressure is less than atmospheric by an amount equal to the magnitude of the negative pressure. During inspiration, this may be as much as −30 to −40 mm Hg, but, in general, it ranges between −3 and −9 mm Hg.

FLOW CHARACTERISTICS. The motion of fluids in tubes may be of two types, laminar and turbulent. In the former, the fluid particles move in straight paths, with the maximum velocity in the center of the vessel, where friction is least, and are stationary in the most peripheral layer, where friction is greatest. The velocity profile is therefore a parabola. If the mean velocity of flow exceeds a critical value indicated by a Reynolds number of 2,000, the fluid particles will no longer travel in stream tubes, but in random paths with constantly changing velocities, although the fluid as a whole may progress at a constant velocity. This is turbulence, and when it occurs, the fluid tends to move more as a solid mass and the velocity profile becomes rounded or square. The Reynolds number (Re) approaches 2,000 in the aorta, where under conditions of minimum viscosity and maximum velocity during the phase of rapid ejection flow may be turbulent. In smaller arteries, the diameters and velocities yield values for Re well below the critical value of 2,000. Therefore turbulent flow is believed to occur rarely in the circulatory system.

While such considerations are valid for continuous tubes, the insertion of branches at various angles may tend to upset the stability of flow in the direction of eddy currents and turbulence. Such a condition may produce drag forces and other phenomena tending to increase frictional effects on the inner surface. Traumatic effects on platelets may also occur because of unstable flow conditions and may produce a tendency toward the deposition of fibrin, a factor which may also lead to plaque formation.

Taxon has recently applied the Bernoulli theorem to blood flow to explain the formation and distribution of atheromatous plaques in the coronary artery circulation. The theorem states that fluid in motion possesses energy by virtue of its velocity and pressure. Flow in a tube with converging boundaries causes the static pressure to be reduced at the narrow portion where the velocity pressure is increased. In curvilinear motion the varying increase in static pressure is greater along the outside curvature by virtue of centrifugal force. Furthermore, since the velocity of flow is greatest at the center, the impingement of the central tube stream upon a site of bifurcation causes an increased velocity pressure and reduced static pressure at the medial wall of the crotch zone. According to Taxon, the first condition may

pertinent; in these, the small intramyocardial arteries as well as the larger extramyocardial vessels show an involvement with atheromatous plaques. We have observed this pattern only occasionally in human cases, usually in familial hyperlipemia. When lipid-containing lesions are uniformly distributed throughout all segments of the coronary circulation, the role of serum lipids appears significant. Such an occurrence, however, is relatively infrequent. The typical distribution of arteriosclerosis of the coronary arterial system is difficult to explain on the basis of elevated serum lipids. In general, as Duff has pointed out, the process in the experimental animal appears to be one of saturation of depots capable of storing lipids, following which there is a rather uniform distribution through the entire arterial system.

There are, however, certain clinical states of *hyperlipemia* in which there appears to be an increased frequency of coronary arteriosclerosis and thrombosis. The most clear-cut examples of such an association occur in *nephrosis* and also in *familial hyperlipemia and hypercholesterolemia*, the genetic aspects of the latter two have been worked out by Adlersberg. There is some disagreement concerning simple biliary obstruction with hypercholesterolemia, hypothyroidism, and diabetes mellitus, duration of disease may be an important factor in the first two of these. It appears that *diabetic patients with hypercholesterolemia* are fifteen times as likely to develop arteriosclerosis as diabetic patients with normal cholesterol levels, but in general, the regulated diabetic does not show hypercholesterolemia or hyperlipemia. Nevertheless, statistical studies showing that myocardial infarction is considerably more frequent among diabetics than in the general population are rather convincing. On the other hand, it would appear that the widely prevalent vascular complications in diabetes cannot be attributed to abnormalities in lipid metabolism alone. Studies supporting the concept of a specific *diabetic angiopathy* involving more than the retinal vessels and renal glomeruli are accumulating, and these suggest a disturbance in polysaccharide metabolism. The arteries involved are usually small branches, suggesting that vascular complications may be due to impairment of communicating branches necessary to establish a collateral blood supply. It is pertinent that the author's studies have not been able to demonstrate an intensification of the arteriosclerotic process in the coronaries or other large arteries when diabetes is uncomplicated by hypertension.

With respect to differences in cholesterol transport between atherosclerotic and normal individuals, such studies have had to be bolstered by statistical techniques because the differences between the two groups were small. Page et al. have been unable to establish a significant rise in serum cholesterol with age, although there is no doubt that the frequency and severity of the arteriosclerotic process increases with advancing years. The studies of Gofman et al. dealing with an abnormal concentration of a specific cholesterol-bearing *lipoprotein* in coronary artery disease, in which the authors believe that the correlation is better than with total serum cholesterol or chylomicronemia, are also in doubt.[4] However, results have been reported which are diametrically opposed to those of Gofman. Furthermore, Paterson has failed to obtain any obvious correlation between the antemortem serum levels of cholesterol, specific lipoproteins, or cholesterol-phospholipid ratio and the degree of sclerosis or the lipid content of human coronary arteries after death.

Edwards et al. have again drawn attention to *sex differences* in the frequency and severity of coronary arteriosclerosis and the implication of hormonal influences. It has been observed that the degree of coronary sclerosis in bilaterally oophorectomized women is greater than in uncastrated females, but less than in men. Furthermore, the incidence of severe coronary arteriosclerosis is 10 to 45 per cent greater in oophorectomized women than in other women of like ages. The most common site of predilection is the anterior descending branch of the left coronary artery, but in 25 per cent of bilaterally ovariectomized females, more severe arteriosclerosis occurs in the middle or distal segments than proximally. The degree of sclerosis does not appear to vary greatly with the nutritional state.

Barr believes that there are distinct sex differences in lipoprotein patterns and that, following ovariectomy, the female pattern is transformed to the male type. He further believes that this has an effect on the coronary

[4] See Part 15, Chap. 4. *Editor.*

during systole. In this way, the coronary system is protected from the sudden ejection by the heart of a mass of blood; it may also account for the infrequency of intense plaque formation at the coronary ostia. Nevertheless, the flow of blood in the coronary system is intermittent, and the stream presents rapid changes in pressure and velocity. With the anatomic characteristics of rapid tapering in the extramural coronary arteries, reflections and eddy currents commonly occur. In addition, flow and pressure, and hence resistance, fluctuate not only with each cardiac cycle but also in response to a variety of other stimuli, including respiration.

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With respect to differences in cholesterol transport between atherosclerotic and normal individuals, such studies have had to be bolstered by statistical techniques because the differences between the two groups were small. Page et al. have been unable to establish a significant rise in serum cholesterol with age, although there is no doubt that the frequency and severity of the arteriosclerotic process increases with advancing years The studies of Gofman et al. dealing with an abnormal concentration of a specific cholesterol-bearing *lipoprotein* in coronary artery disease, in which the authors believe that the correlation is better than with total serum cholesterol or chylomicronemia, are also in doubt.[4] However, results have been reported which are diametrically opposed to those of Gofman. Furthermore, Paterson has failed to obtain any obvious correlation between the antemortem serum levels of cholesterol, specific lipoproteins, or cholesterol-phospholipid ratio and the degree of sclerosis or the lipid content of human coronary arteries after death

Edwards et al. have again drawn attention to *sex differences* in the frequency and severity of coronary arteriosclerosis and the implication of hormonal influences. It has been observed that the degree of coronary sclerosis in bilaterally oophorectomized women is greater than in uncastrated females, but less than in men. Furthermore, the incidence of severe coronary arteriosclerosis is 10 to 45 per cent greater in oophorectomized women than in other women of like ages The most common site of predilection is the anterior descending branch of the left coronary artery, but in 25 per cent of bilaterally ovariectomized females, more severe arteriosclerosis occurs in the middle or distal segments than proximally. The degree of sclerosis does not appear to vary greatly with the nutritional state.

Barr believes that there are distinct sex differences in lipoprotein patterns and that, following ovariectomy, the female pattern is transformed to the male type. He further believes that this has an effect on the coronary

[4] See Part 15, Chap. 4. *Editor.*

great as between media and adventitia Such shearing effects are believed to occur particularly when part of the vessel wall is anchored to an adjacent structure, as for example, the suspending bands which bind the abdominal aorta to the vertebral column Duguid believes that such attachments produce a drag leading to splits and chinks which tend to separate the vascular tissue layers from each other.

The observations of Whitten, previously mentioned, are particularly pertinent here since they serve to explain in part the greater susceptibility of the left coronary system (with its fixed branches) to shearing forces In fact, the observed buckling of the vessel at such points of fixation may be the result of such shearing effects This situation is comparable to one pointed out by Willis in the aorta, which elongates with each cardiac cycle and becomes distended, there is then a tugging of the intercostal vessels which is released in diastole, leading to a loss in both circumferential and longitudinal elasticity, with resultant dilatation and buckling.

The role of hemodynamic forces in the pathogenesis of degenerative vascular disease derives its strongest support, then, from direct observations on human postmortem material along with a correlation with recognized physiologic phenomena It suffers particularly from a lack of experimental reproduction In large part this is due to a difficulty in setting up experimental conditions which reproduce or intensify known operating hemodynamic conditions This area of investigation needs considerable development

EFFECTS OF CORONARY ARTERY DISEASE ON CARDIAC STRUCTURES

Certain tissues such as cartilage, the lens of the eye, the cortex of the tooth, and the middle third of artery walls are able to function without a blood supply, presumably because permeability conditions are adequate to provide them with nutrients In the case of the vessel wall, the inner third receives its nutrition by permeation through the endothelium and through stomata in the endothelial lining, while the outer third is supplied by the vasa vasorum This situation is temporary for, as the vessel wall thickens, permeability factors become insufficient to supply the middle third and vascularization of the wall takes place As Winternitz has shown, ramifications of the adventitial vasa extend into the media and anastomose freely with vessels of capillary size originating in ostia in the endothelial lining. Diffusion mechanisms apparently remain adequate as long as the wall remains below a certain critical thickness, and the development of a vascular plexus thus constitutes a response to progressive thickening from any cause; it is, perhaps, stimulated by local hypoxia in areas most distant from a vascular supply.

While such changes in vascular walls can properly be considered part of the arteriosclerotic process, complications which develop because of their presence may have serious consequences. As the artery wall is compressed between the lateral pressure within the lumen and the tough inelastic adventitia, this intramural plexus is subjected to considerable stress *Hemorrhages of the intramural vessels* may occur, and as Paterson and Wartman have demonstrated, *occlusion* may follow such bleeding into intimal plaques While Paterson has reported such hemorrhagic foci at the site of thrombotic occlusion in 31 of 36 consecutive cases, others have found them less frequently The incidence of such a finding is apparently dependent upon the diligence with which it is sought In addition, Wartman has pointed out that such hematomas may be of sufficient size as to cause occlusion of the lumen without the added factor of intraluminal thrombosis It is also recognized that hemorrhage into atheromatous lesions of the coronary artery without obstructing the lumen may precipitate *acute coronary insufficiency*

Collateral Circulation. According to Zoll, Wessler, and Schlesinger, only about 9 per cent of normal hearts have demonstrable collateral channels in addition to the direct linear path of the coronary circulation The occurrence of complete coronary occlusion or severe narrowing of one or more coronary arteries without evidence of myocardial infarction is usually attributed to the fact that the slow progress of the obstructing lesion allows sufficient time for the formation of an *adequate collateral coronary circulation* In fact, Karsner has stated that he has not observed infarction to result from gradual occlusion of the coronary arteries by arteriosclerosis.

Such observations imply that the development of collateral coronary channels is a response to coronary artery insufficiency and di-

the following: (1) blood pressure–hydrostatic tension; (2) cardiac thrust; (3) vibration; (4) gravity effect–static pressure; (5) flow characteristics; (6) viscosity, friction; (7) shearing forces.

BLOOD PRESSURE–HYDROSTATIC TENSION. Most observers agree that the arteriosclerotic process in the coronary arteries is intensified in hypertensive states, although Lee and Thomas were unable to find a significant correlation between kidney weights and groups with and without myocardial infarction. In the Negro race the severity of coronary arteriosclerosis and the incidence of myocardial infarction are considerably less than among Caucasians, although hypertension is more prevalent. However, blood pressure also appears to be an important factor even in normotensive individuals, the basic difference being the time factor. It is the latter which has led many investigators to consider hemodynamic structural responses as an aging phenomenon. Moschkowitz has expressed the role of blood pressure by the equation: arteriosclerosis = intravascular tension × time.

In this regard, the observations previously noted on the development of arteriosclerosis in anomalous coronary vessels originating from the pulmonary trunk are particularly pertinent. Kaunitz has observed that, in the adult heart in which the left coronary artery arises from the pulmonary trunk, the lack of arteriosclerosis in such a vessel coupled with arteriosclerosis in the right coronary would seem to indicate a relationship between intravascular pressure and the development of arteriosclerosis.

Winternitz pointed out that, when pressure within the lumen is increased, the intima and media become compressed between this force and the tough outer adventitial coat, with concomitant compression of the intramural capillary bed; such impairment of the latter may then lead to degenerative changes in the arterial wall and atheroma formation. Since the intravascular tension diminishes with the decreasing caliber of arteries, as does the requirement for an intramural circulation, it would be expected that such a process should be more intense in large vessels, and this is in agreement with observations.

Vascular size may also have an influence in another way, since it determines the hydrostatic tension existing in a given artery. Tension is basically an expression of the stretching force excited by the hydrostatic pressure on the vascular wall. This force in turn is counteracted by the tension developed in the wall tending to diminish its diameter. The latter consists of three main components, i.e. elastic tension, active or muscular tension, and interfacial tension. Burton has shown that the hydrostatic tension in any vessel may be calculated by applying the classic law of Laplace, $T = P \times R$, in which P is the excess of hydrostatic pressure inside the vessel over the local surrounding tissue pressure, T the tension developing in the wall, and R the radius of the vessel.

An application of this principle to operating conditions in the arterial system has shown that, in general, there is a direct correlation between the operating tension of a vessel and its susceptibility to arteriosclerosis. This is so, too, within a particular unit of the system, such as the coronary or cerebral circulation. Further, it explains why the intramyocardial segments of the coronary system fail to develop significant sclerosis in the large majority of cases of coronary heart disease, since the diameters of such segments are small and the difference between the intravascular and the local surrounding pressures is smaller than where arteries are surrounded by softer structures. It also explains, in part at least, the difference in susceptibility of the two coronaries, since the left coronary arteries are larger, deeper penetrating, and more rigidly fixed at points of branching than those of the right side of the coronary system. Certain of these anatomic differences are also important in considering the effects of shearing forces, eddy currents, and turbulence.

The fundamental Laplace equation has been modified by Willis to take into account also curved vessels; he has shown that the hydrostatic tension is highest along the inner curvature of a vessel, as is also the intensity of the arteriosclerotic process. The predilection of plaque formation for sites of branching of arteries can also be explained on the basis of the Laplace equation. At the origins of many branches, there is an "Indian-club" type of expansion, thus providing a larger radius than in more distal portions of the branch. Furthermore, there is a normal progressive dilatation, always occurring at the approach to a major bifurcation, which also is a common site of intensified plaque formation. Also, at the point of origin of a branch, the hydrostatic pressure is that of the parent trunk, and the tension requirement would likewise be that of the latter; but the structural characteristics are those of the branch which shows an abrupt diminution in the number of elastic fibers in the coronary arteries and a corresponding loss of ability to develop elastic tension; this, therefore, results in a loss of efficiency in the development of intramural tension.

CARDIAC THRUST. The foregoing considerations do not take into account the pulsating pressure created by the ventricular pump. The coronary arteries appear to be unique with respect to phasic variations in blood flow since there is increased flow during diastole and markedly reduced flow

tricle may lead to some degree of myocardial hypertrophy, but that it is usually not of severe degree. Harrison and Wood believe that the severity can be correlated with the duration of heart failure. Boas and Boas also believe that patients with a normal blood pressure under observation for years develop progressive cardiac enlargement following myocardial infarction, all these patients have had one or more episodes of heart failure following the infarction.

Myocardial Degeneration. *Focal necrosis* of the myocardium may occur whenever there exists a chronic deficiency of oxygen in the blood delivered to the myocardial fibers. Coronary artery narrowing from whatever cause is probably the most common finding related to such a state Other causes include circulatory shock, aortic insufficiency, severe anemia, subacute carbon monoxide poisoning, breathing of air with reduced oxygen content (as at high altitudes), massive pulmonary embolism, and chronic ventricular hypertrophy without decompensation These other causal factors may be sufficiently effective, even at diminished intensity levels when the coronary artery supply is insufficient.

The necrotic foci of muscle are of microscopic size, showing first a loss of striations of the fibers, then coagulation of sarcoplasm into a homogeneous mass accompanied by shrinking of the nuclei The latter then disappear, and in the course of about 24 hr, the necrotic fibers become infiltrated with polymorphonuclear leucocytes, and the necrotic material is then liquified and readsorbed Local connective tissue cells then proliferate, and eventually the necrotic focus is replaced by fibrous tissue, forming a small scar

A comparable lesion has been described by Schlesinger and Reiner It is found most frequently at the borders of myocardial infarcts; frequent sites in hearts without infarcts are the central portion of papillary muscles and trabeculae carneae of the left ventricle, these centers are at the ends of the pure coronary vascular circulation where metabolic exchange partly occurs by transendocardial diffusion It is suggested that the lesion may result from metabolic imbalance in the heart, e g, abnormalities of tissue anabolism and catabolism due to ischemia, anemia, hypotension, hypoglycemia, septicemia, toxemia, heart failure, cardiac dilatation, and nutritional disturbances. They prefer the term *focal myocytolysis* to hypoxic necrosis or miliary infarction, since the process appears to be slower in evolution than infarction, is due to a lesser degree of metabolic imbalance than miliary infarct, and is more common

Dock has described another process of myocardial degeneration to which he has applied the term *presbycardia* to indicate myocardial senescence He believes that, in older patients without significant coronary artery disease, this condition may lead to heart failure. While the accumulation of brown pigment in myocardial fibers in aged individuals is common (*brown atrophy*), it is not believed to be related to this condition since, according to Harrison and Resnick, there appears to be no recognizable histologic basis and no known clinical defect to account for this process of presbycardia

Myocardial Infarction. It is commonly accepted that 90 to 95 per cent of myocardial infarcts result from coronary sclerosis Approximately one-half of these are associated with *thrombosis*, one-fourth with *sclerotic occlusion*, and one-fourth with *both*. In most cases, all three main coronary channels show some degree of arteriosclerosis On the other hand, Bean has observed that, in as many as 20 per cent of cases of myocardial infarction, the coronary arteries show sclerotic narrowing but no occlusion According to Wartman and Hellerstein, 3.8 per cent even fail to show significant coronary sclerosis, these usually occur in patients with cardiac hypertrophy and hypertension, and some observers believe that infarction is due to *prolonged myocardial ischemia* (Fig 10-4).

There are also cases of sudden death, presumably from a "heart attack," in which the coronary arteries are relatively free of disease and no myocardial infarct is found, in most of them the left ventricle is greatly hypertrophied Other cases with a similar clinical history may show a severe degree of arteriosclerosis of the coronary arteries at one or more points, or diffusely, but without myocardial infarction. In Yater's series, 10 per cent of cases of sudden death were in the latter categories. In general, although coronary artery sclerosis is a common finding in cases of sudden death (40 to 79 per cent in various

account for intimal thickening generally, while the latter two events would explain the susceptibility to plaque formation on the inner curve of a tortuosity and at the bifurcation of arteries, respectively.

Taxon's use of the term "suction" to express pressure differences between two points is unfortunate, since this implies an ability to pull away the inner layers from the remainder of the wall. Such pressure differences, if of sufficient magnitude, would more likely cause a collapse of the total wall, an event which Taxon apparently realizes only to the extent that it would intensify the reduction in central static pressure On the other hand, the magnitude of such pressure differences in arteries is unknown. If they are significant, the extent to which they would be effective would depend upon the resistance to vascular collapse supplied by external attachments of arteries to adjacent structures. Where such attachments occur, the most loosely attached structures within the wall might be moved toward the center of the vessel. On the other hand, rather than an imparting of motion to definite structures of the arterial wall, the effect might be one of moving ground substance and fluid constituents which might then, over a period of time, cause degenerative changes in the cellular and fibrous structures But this too would depend upon the magnitude of such pressure differences and their frequency of fluctuation In general, then, there is a need for demonstrating that the Taxon concept applies to resilient structures, such as artery walls; whether the pressure differences are of sufficient magnitude to be significant, and what effects they produce on vascular structures.

VISCOSITY—FRICTION Plastic flow represents a true interaction between the walls of a tube and the particles flowing through it, by contrast, in viscous flow the interaction is solely between the layers of the fluid itself, the layer nearest the wall of the tube being stationary. Flow in arteries is of the viscous type Changes in vasomotor tone may be produced by alterations in the viscosity of the blood as well as by increase or decrease in the extravascular pressure exerted upon the blood vessels, such as occurs in the coronary arteries of the heart during systole.

The relative viscosity of blood at 37°C varies normally from 2 5 to 4 times that of water However, the viscosity of blood is a tricky component to evaluate in the body and is entirely different from that predetermined in vitro. It seems probable that, in vessels of large diameters (10 times or greater than the diameter of a red cell) and at low velocities, fluid tends to remain an evenly distributed suspension with normal viscous properties but that, at greater velocities, the cells are thrown into the center of the stream where they move as a mass, leaving a layer of relatively cell-free low-viscosity plasma near the wall, which gives an over-all reduced viscosity measurement. The more viscous central stream might serve to reduce static pressure differences, and this factor Taxon failed to consider.

Mendlowitz pointed out that *viscosity* is also important in determining intravascular resistance. The latter is determined by the vector of the frictional forces in the blood opposing the driving mean pressure. When volume flow is constant, these forces are in equilibrium, and mean frictional resistance should be exactly equal to mean pressure. Frictional resistance is equal to the pressure multiplied by the mean cross-sectional area of the vessel and is directly, rather than inversely, proportional to flow.

If the apparent viscosity of the blood in vessels is increased, the relationship between pressure and flow becomes curvilinear, with the convexity of the curve toward the pressure axis. This is probably a physical phenomenon dependent upon the distribution of cells and plasma in the flowing stream. With decreasing vascular caliber, the apparent viscosity decreases until a critical level is reached, when it increases again With increasing velocity, viscosity decreases until a critical level is reached, when it becomes steady. Another factor is blood temperature, which causes an inverse change in viscosity.

It is apparent that these relationships are complex, one of the important factors being the size of the plasma "rim" of the flowing stream Plasma is less viscous than whole blood, and a greater proportion of the shearing stress of laminar flow occurs in the rim than in the center of the vessel.

While such factors as viscosity and friction are thus difficult to evaluate, they might be expected to exert influences on vascular structures in two ways, i e., by an effect on the endothelial lining and intervening ground substance, thus influencing nutrition and permeability, and possibly by offering a resistance to the normal pulsatile motion of the artery wall in some areas

One disease in which viscosity appears to play a role is *polycythemia vera* The increase in viscosity appears to enhance the formation of intravascular thrombi. Whether this is due to changes in the physical characteristics of the blood per se or to some secondary effect on vascular lining cells and ground substance is not known.

SHEARING FORCES. The idea that shearing forces may play a role in initiating degenerative processes in arteries was first proposed by Albutt who stressed particularly slip between intima and media during contraction and dilatation. Later Krafka showed that slip in this area is not so

he area of infarction is large, particularly if the arteriosclerotic process is not advanced. When the occlusion develops slowly, there may be little or no infarction since adequate collateral circulation may have developed. Factors determining the formation of a collateral system have already been discussed If two major channels are blocked, then even a well-developed collateral system may not suffice to prevent infarction Such a condition, if not simultaneous, may lead to *infarction at a distance*. Thus if a first coronary artery is blocked and no infarction results because of adequate collateral circulation, and then a second vessel is subsequently also occluded, the area of infarction may correspond to the distribution of the first artery.

The condition of the heart muscle is related not only to the state of the small intramyocardial branches but also to the presence and degree of *cardiac hypertrophy*, since the latter process may result in a disproportion of myocardial mass to vascular channels The importance of *age* in relation to the development of anastomotic channels derives from the fact that, the older the patient, the greater and freer are the anastomoses likely to be and the less likely it is that a myocardial infarct will develop if a single channel is occluded As previously mentioned, progressive sclerotic narrowing of coronary arteries appears to act as a stimulus to the development of collaterals, and such sclerosis is generally more advanced in older individuals

The normal relative thickness of the myocardium may also determine its susceptibility to infarction Schlesinger has pointed out the *rarity of infarction of the posterior basal portion of the right ventricle* despite the relatively frequent occlusion of the right coronary artery This is also true of the *atria* Such thin-walled areas may derive considerable nourishment by direct diffusion from blood within the cardiac chambers The range of frequency of atrial infarcts in various reports is between 8 5 and 42 per cent of cases with myocardial infarction It is generally agreed that about 1 per cent of all hearts examined at autopsy contain infarcts of the atria Of these, about one-fifth show *only atrial involvement*, and the remainder are associated with ventricular infarcts Mural thrombi are present in most of the cases, thus probably excluding diffusion of nutrients into the atrial musculature. *Infarction of the right atrium* is much more common than the left, probably for two reasons: (1) mural thrombi of the right atrium are usually associated with coronary heart disease, while involvement of the left atrium is usually associated with rheumatic heart disease; (2) the resistance of the left atrium to myocardial infarction may be attributed to the high oxygen tension of the blood in its chamber. Ventral infarcts of the right atrium usually involve the *auricle*, while dorsal ones are usually an extension of a posterior right ventricular infarct.

Factors which may precipitate coronary thrombosis, myocardial infarction, or both are increased viscosity of the blood as in polycythemia *vera*, *effort*, *emotion*, exposure to low temperature or low oxygen tension (as at high altitudes), infections, spontaneous and insulin *hypoglycemia*, *indirect trauma*, operative trauma, anesthesia, hemorrhage and shock, overeating, serum sickness, and excessive heat and humidity.

If death occurs within a few hours after the onset of the acute attack, no gross or microscopic changes in the myocardium will be evident The earliest detectable gross changes occur about *4 to 6 hr* after onset and consist of a pale, dry, swollen irregular area in the affected myocardium. During this time, the myocardial fibers show a hyaline change in the cytoplasm with loss of cross-striations and a developing *pyknosis, karyorrhexis, and karyolysis* of nuclei

From about 6 hr to approximately *7 days*, *gross characteristics consist of* a deep-red area of hemorrhage (if the infarct is hemorrhagic) or a clay-colored appearance with a hemorrhage *periphery and an outer yellow* margin (if the infarct is of the anemic type). These alterations have a streaky arrangement if the infarct is patchy Microscopically, there is frank necrosis of muscle fibers, connective tissue, and smaller blood vessels, large areas of *hemorrhage are* present within the affected area in a hemorrhagic infarct, or numerous small foci around the periphery *in an anemic infarct* The *outermost* zone shows fatty degeneration of muscle Infiltration of *polymorphonuclear* leucocytes begins at about 5 to 6 *hr, increases slightly* over the next *18 hr*, following which there is a progressive increase

minished myocardial oxygenation. There is no significant formation of such collaterals until narrowing of the coronary arteries exceeds 75 per cent of the lumen diameter; at this point, about 58 per cent of hearts have a demonstrable collateral circulation. With complete acute occlusion, the frequency is about 80 per cent, and with complete chronic (atheromatous) occlusion, the incidence increases to 100 per cent (Fig. 10-3).

Beck and Brofman also believe that the stenosing process of the coronary arteries is ineffective in the production of collateral channels until it becomes severe, but the process apparently does not proceed at an equal rate in all patients with a comparable degree of narrowing Coronary insufficiency without the development of adequate collateral is believed by many to be responsible for cardiac arrhythmias, with resulting intracardiac thrombosis and other complications. Such cardiac irregularities may even develop in individuals with degrees of narrowing of less than 75 per cent.

The presence or absence of an adequate collateral system may thus constitute a critical determinant as to whether or not an individual will survive an acute coronary occlusion. A distinction as to the etiologic type of coronary arteriosclerosis thus becomes of practical importance since an inflammatory or metabolic process involving small intramyocardial branches may lead to obliteration of channels bridging the primary and collateral systems This consideration may serve to explain why initial coronary occlusions are so often fatal in young individuals and perhaps in diabetics, where these two etiologic types of coronary artery disease are prevalent.

Cardiac Hypertrophy. The problem as to whether coronary artery disease of itself can cause cardiac hypertrophy remains controversial. It is complicated by the fact that, while about one-third of persons with coronary occlusion have cardiac hypertrophy, preexisting hypertension favors the development of coronary sclerosis both as to frequency and severity, and approximately 40 per cent of coronary occlusions occur in individuals with an antecedent history of hypertension.

Aschoff, as well as Kaplan et al., stated that coronary artery disease per se causes no significant hypertrophy. French and Dock have been unable to demonstrate significant hypertrophy in the hearts of young men with coronary artery disease. On the other hand, Davis and Blumgart have reported that coronary sclerosis may lead to cardiac hypertrophy, presumably because impaired nutrition to the myocardium induces stretching and hypertrophy of fibers. Karsner has stated that hypertrophy occurs in infarcted hearts independently of hypertension, again caused by stretching of the remaining living muscle. In a study of the [illegible] weight of [illegible] onary disea[illegible] that coronary [illegible] left ventricular hypertrophy

Some proponents of this association believe that, when coronary occlusion leads to heart failure, the subsequent dilatation of the ven-

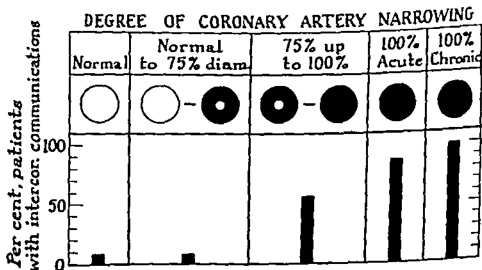


Fig. 10-3. Presence of intercoronary arterial anastomosis in human hearts with various degrees of stenosis. (From Zoll et al. Circul. 1951.)

of heart rupture among routine *autopsies* in general hospitals is about 0.35 per cent. The incidence is higher among coroner's cases since *cardiorrhexis* is a frequent cause of sudden death, especially after myocardial *infarction*. The incidence is also higher in mental institutions. Among autopsies revealing a myocardial infarct, the incidence of heart *rupture* is 4.4 per cent. However, in acute *myocardial* infarction, the incidence is about 9 per cent.

Rupture from a transmural myocardial infarction usually develops *between the fourth and eleventh day* after onset of the infarction, although it may occur as late as the twenty-first day. *Mallory* believes that it does not occur after the third week. According to Wessler *et al.*, there appears to be a uniform pathologic substrate common to hearts with spontaneous rupture. This consists of an acute coronary occlusion with recent transmural myocardial infarction, the infarcted area is poorly supplied by collaterals, and fibrosis is entirely absent in at least one area. These hearts, therefore, appear to be totally unprotected by scar or anastomoses at the site of acute infarction. The time lag between onset of infarction and rupture is probably explained by progression of peripheral myocytolysis until the infarct becomes truly transmural. Typically, this catastrophe occurs in patients who are hypertensive but have no previous history of infarction or congestive failure. Only rare instances of rupture through an old scar have been reported. The precipitating incident appears to be a sudden increase in intracardiac pressure or excessive effort after recent infarction. The use of levarterenol in myocardial infarction associated with shock, or anticoagulant therapy, does not appear to increase the frequency of this complication.

Rupture of the heart is more common in women than in men. About 90 per cent of ruptures occur *through the external ventricular wall*; of these, about 80 per cent occur through the left, and about 10 per cent through the *right ventricle*. The right atrium is involved in *about 6 per cent* of external ruptures, and the left about half as frequently. About *100 cases of rupture of the interventricular septum* have been reported, a third of which have been diagnosed antemortem; this lower incidence is believed to be due to the more anastomotic coronary circulation in the interventricular septum. Survival with an interventricular *rupture usually* varies from several hours to several days, but sometimes survival is as long as several months or years. Wood and Livezey reported the case of a patient who lived almost *5 years* following this complication.

SPONTANEOUS RUPTURE OF A PAPILLARY MUSCLE. Rupture of a papillary *muscle* occurs less *often* than rupture of a cardiac wall. It is *most often* a complication of a myocardial infarct in which the muscles of the left *ventricle* are involved. It is *encountered* in rare instances as a result of bacterial vegetations on the papillary muscles of the right ventricle or in association with syphilis. In the left ventricle, the posterior muscle to the mitral valve is affected about twice as often as the anterior, presumably because of a poor collateral blood supply, and perhaps also because of a poor collateral blood supply to the superficial bulbospiral muscle which forms the left posterior papillary muscle. Such rupture is most often associated with *thrombosis* of the *right* coronary artery or *the* circumflex branch of the left coronary artery.

The antemortem diagnosis of rupture of a papillary muscle is rarely made. However, in typical cases, a murmur develops following the onset of pain. The torn muscle may at first produce no unusual murmur, but as it becomes twisted and tangled in the chordae tendineae, it may set up extraneous heart sounds. The cause of this lesion is believed to be excessive strain on the necrotic muscle, and this appears particularly applicable to those cases with a thickened mitral valve, shortened chordae tendineae, and hypertrophied myocardium. Most patients die suddenly after such an event, but one case reported survived for as long as 20 months. Acute mitral insufficiency results from severance of the papillary muscle, with development of pulmonary edema which *is immediate* and progressive, dyspne becomes increasingly marked, and cyanosis appears.

CARDIAC ANEURYSM. A cardiac aneurysm is a bulging of a diseased wall in response to intraluminal pressure. Such a bulge may be *noted during the acute stage* of an infarct or *observed as the thin fibrous sac* of an old *healed scar.* The term is probably better reserved for the latter situation *since the former*

reports), myocardial infarction (old or recent) is found in only about one-third of cases.

The incidence of myocardial infarction in various autopsy series has ranged from 1 to 9 per cent, with the corrected ratio of men to women of about 1.3:1. While the ratio of male to female is often stated to be about 3:1, the male preponderance disappears in older age groups, where in some series there has even been reported a slight female preponderance Furthermore, there appears to be no sex difference in diabetic patients.

Myocardial infarction has been observed in the *newborn* and in *infancy*, where it has been related either to trauma to the coronary arteries incident to birth or to a peculiar sclerosing disease of the coronary arteries, in which calcification is a considerably more prominent feature than later in life. Severe coronary sclerosis with occlusion and myocardial infarction also occurs in *early childhood* in familial hyperlipemia and xanthomatosis. Myocardial infarction in *women under 40* appears to be rare except in association with obesity, hypertension, or hyperlipemia. It is also uncommon in *men under 30*, but in the latter part of the fourth decade it is about thirty times as frequent as in the third decade.

Myocardial infarction is the result of sustained, relatively severe myocardial ischemia In most cases, this is caused by coronary occlusion which may be (1) sudden as in *embolism*, (2) relatively sudden as in *thrombosis* (especially when the latter results from hemorrhage into a plaque or into the lumen of a vessel), or (3) gradual as in *sclerotic occlusion without thrombosis*. The following factors are important in determining whether or not an infarct will develop: (1) size and location of the obliterated vessel, (2) duration and rapidity of obliteration, (3) condition of the general circulation and of the heart musculature, (4) age of the individual

If the occlusion of a main branch is *sudden*,

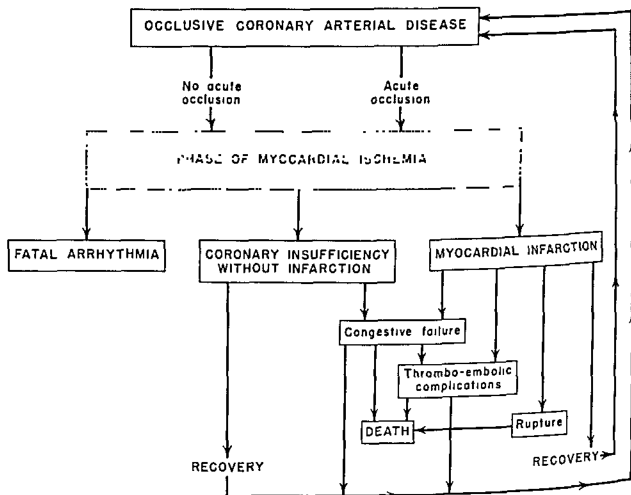


Fig. 10-4. The spectrum of occlusive coronary artery disease. (*From Edwards Tufts M. Alumni Bull.* 1952.)

3

Clinical aspects of coronary heart disease

CHARLES W. CRUMPTON

Coronary artery disease is characterized pathologically by intimal atherosclerosis producing narrowing of the lumen and frequently occlusion, physiologically, by a reduced oxygen tension of the myocardium resulting from a disproportion between oxygen supply and demand, and clinically, by variable manifestations ranging from mild chest pain to myocardial infarction, which may be followed by congestive failure or sudden death Thus, *coronary heart disease* is a clinical term for a number of syndromes which result from myocardial ischemia On the other hand, it is well known to pathologists that severe grades of coronary atherosclerosis are not incompatible with good health and normal heart action while lesser grades of disease may be associated with occlusive phenomena Extensive pathologic lesions involving the coronary arteries may be present but cannot be diagnosed unless they produce overt clinical manifestations There is evidence to suggest that coronary atherosclerosis may be present in the majority of the population, but it is not recognizable as disease until symptoms develop This disease is further complicated by the fact that the patient's history is still the most reliable means of suspecting the presence of significant disease of the coronary arteries

EPIDEMIOLOGY OF CORONARY ARTERY DISEASE

There is mounting evidence that atherosclerosis and its principal complication, coronary artery disease, are related to the *mode of life*, and there is growing interest, therefore, in the possible contributions epidemiology might make in unraveling the many problems involved (Morris, 1958)

It is a clinical commonplace that there are *multiple causes* of disease. Thus, there may be a sole or rather crucial cause of coronary artery disease, but, in the absence of any such evidence, experience suggests that it is unwise to assume so.

It is not merely academic to ask whether there are *multiple causes of coronary heart disease* In the long journey from atheromatous flecking of a coronary artery to the fatal case of coronary artery disease, several distinct causes may be operating, and some may be more controllable than others (Morris, 1958, Benton et al , 1954)

Constitutional factors are important in coronary heart disease, but there is also evidence of variation of its incidence with *environment*. In addition, its relationship to *physical effort* is highly controversial, in many instances with significant medicolegal connotations. Whatever the influence of the precipitating factors, it is agreed that preexisting intrinsic coronary artery disease must be present.

With reference to *psychosomatic factors* in the pathogenesis of this disease,[1] it is of interest to note that there have been described increased capillary permeability and hemor

[1] See Chap 1 and Part 17, Chap. 1. *Editor.*

in leucocytic infiltration to a maximum at about the fourth day. By *the fifth day* the leucocytes *begin to undergo necrosis and then gradually disappear.* From the fourth day on, eosinophiles appear in the infarct area. An ingrowth of capillaries and connective tissue to organize the infarct also begins at about the fourth day.

At the end of *the first week,* the gross infarct has developed a dark-brown color, the center becomes depressed, and this zone becomes progressively wider and paler. Correspondingly, on a microscopic level, processes of organization progress; pigmented macrophages containing either hemosiderin from the hemorrhage or lipofuscin from necrotic muscle appear about the sixth day. At about *the tenth day,* a peripheral 1-mm rim of necrotic muscle has been removed, and lymphocytes and plasma cells appear to reach a maximum concentration at about the third week. Infiltration of eosinophiles reaches a maximum at approximately the eighteenth day. By about *6 weeks* most of the necrotic muscle has been removed, although some may still be present. *Collagen first appears* in organizing areas at about the twelfth day and is quite prominent by the end of the third week By the sixth week, there is sufficient collagen formation for contraction to become grossly evident.

Collagen formation reaches a maximum *between the second and third month.* By the end of *a year,* pigmented macrophages, lymphocytes, and plasma cells have all disappeared, and all that remains is *a dense fibrocollagenous scar,* which has replaced the affected myocardium. *Calcification* of necrotic tissue in myocardial infarcts occasionally occurs and may progress to *bone formation*

Wartman and Sonders noted that ventricular infarcts fall into three categories as regards extent of involvement: (1) full thickness; (2) massive, but not full thickness, and (3) laminar or rimlike The superficial bundles are involved, alone or in combination with the deep bundles, in about 74 per cent of myocardial infarcts, and the deep bundles, alone or in combination with the superficial bundles, in 51 per cent The deep sinospiral bundle is involved less often than other layers. Infarcts involving more than one bundle occur with considerably greater frequency than infarcts of a single bundle. Of the cases studied by Wartman and Sonders, 59 per cent showed only one infarct, while 41 per cent showed two or more.

A particular type of *laminar infarct* deserves mention. A number of investigators have reported *large subendocardial infarcts.* It appears that, in a healed stage, these are indistinguishable from so-called subendocardial fibroelastosis, and recent reports of the latter entity may include some healed subendocardial infarcts.

Sequelae of Myocardial Infarction. PERICARDITIS. The incidence of pericarditis following myocardial infarction varies from 15 5 to as high as 80 per cent in various reports. The pericarditis is, of course, the result of extension of the infarction to the epicardial surface It usually appears within the first 24 hr Organization begins at 6 to 8 days and is complete at about 4 weeks.

MURAL THROMBUS. Until the recent use of anticoagulant therapy, mural thrombus was encountered at the site of infarction in about one-half of infarcted hearts. It now appears to be diminishing in frequency. Although *mural thrombi usually form* as a result of extension of the infarct to the endocardium, they may also form as a result of localized dilatation of the infarcted wall. As a rule, such thrombi do not begin to form before the fifth day, organization usually begins at about the ninth day and is complete by about the sixteenth day. According to Bean, they may remain as organized thrombi for as long as 3 years As would be expected, when due to infarction they are most frequently encountered in the left ventricle, less often in the atria, and least often in the right ventricle. Approximately one-third of patients with mural thrombi in the left ventricle develop *systemic embolism,* the most common sites in order of frequency being the kidneys, spleen, lower extremities (femoral), and intestines (mesenteric). Such an event may constitute the immediate cause of death.

RUPTURE OF THE HEART. In recent years, several large surveys have been compiled regarding this complication Such studies have included incidence and *recognition,* association with underlying *heart disease,* timing of rupture after myocardial infarction, association with hypertension, and relation to exertion and to therapy The average frequency

vascularized), but as a complicating factor, it may be highly important. Depending on the size of an intimal hemorrhage, its position within a plaque, and on coronary flow past the point of injury, the following sequelae may be produced.

1. *Coronary artery spasm (speculative).*
2. *Acceleration of the atherosclerotic process:* the addition of blood to an atherosclerotic plaque must increase its bulk.

Single hemorrhagic episodes might produce little effect once the fluid portion of the blood is absorbed, but the gradual accumulation of the solid elements, such as cholesterol and blood pigment, from repeated hemorrhages into the same plaque should perceptibly increase its size. With a larger hemorrhage, there is a distinct possibility that the coronary lumen will be so reduced that symptoms might result. Symptoms which originate in this manner should be transient, and one would expect them to disappear with the absorption of the hemorrhage.

3. *Coronary occlusion from massive intimal hematoma* (less than 10 per cent)
4. *The initiation of coronary thrombi.*

Thus, coronary arteriosclerotic narrowings and occlusions are observed in approximately 90 per cent of patients with coronary artery disease. Since coronary atherosclerosis has been shown to exist in the absence of clinical manifestations of coronary artery disease, the sequelae of this pathologic change, as well as the ability to develop sufficient collateral blood supply to the myocardium, may directly influence the variable clinical course. *Intimal capillary rupture* within the atherosclerotic plaque may be precipitated by three general causes (1) abnormally high pressure within its lumen, (2) abnormal fragility of its wall, and (3) lack of support from the adjacent tissues

Conditions other than coronary atherosclerosis are responsible for cardiac pain in approximately 10 per cent of patients. Arterial *hypertension* and *valvular disease* increase cardiac work and may result in decreased efficiency. *Syphilitic aortitis with aortic regurgitation* or narrowing of the coronary ostia, periarteritis nodosa, thromboangiitis obliterans, rheumatic arteritis, scleroderma, or amyloidosis, increased right ventricular work, such as occurs in *cor pulmonale*, tight *mitral stenosis*, congenital *pulmonic stenosis*, malignant ductus, or ventricular septal defect with pulmonary hypertension, may all cause precordial pain. *Aortic stenosis*, with its frequent distortion of the coronary ostia and the increase in left ventricular work, likewise predisposes to cardiac pain.

SECONDARY PREDISPOSING FACTORS. Men are affected approximately five times as often as women. Coronary artery disease occurs predominantly after the age of 40. Peel found that, in men, the incidence is significantly earlier than in women, reaches a peak at 55 to 59, and then decreases. *In women*, the incidence of occurrence gradually increases from the age of 40 to 70 without fluctuation. Prior to World War II, coronary artery disease in men under 30 years of age was regarded as rare, and in men between 30 and 40 years of age, as uncommon. However, instances of advanced coronary artery disease have been reported in men between the ages of 18 and 39 years, and there is further evidence that the frequency of the disease *in this age group* is increasing (Yater et al.). Gertler reported a ratio of 97 men to 3 women observed in a study of 100 cases of coronary heart disease under the age of 40 years. Thus, the predominant male element in this disease group under the age of 40 is the outstanding etiologic clue (Gertler et al.).

From the clinical standpoint, *familial* occurrence of coronary artery disease has been observed with unwarranted frequency and to a severe degree

Thomas and Cohen studied the familial occurrence of coronary artery disease and hypertension, both singly and combined, as they appeared among the relatives of unselected medical students. Coronary artery disease was nearly four times as prevalent among siblings of individuals with coronary artery disease as among siblings of persons without it. In the search for evidence of causal interrelationships among coronary artery disease, hypertension, obesity, and diabetes mellitus, it was found that combinations of two or more disorders affecting the same individual occurred more frequently among both parents and grandparents than might be expected by chance alone. The degrees of association were particularly high between hypertension and coronary artery disease and between hypertension and obesity.

Gertler and White, in their study of coronary heart disease in young adults, reported that there were more deaths due to coronary heart disease

may be only temporary and disappear following adequate healing. Lack of distinction between these two conditions has led to some confusion, particularly as regards the frequency of this complication. Thus, reports as to incidence in cases of myocardial infarction vary from 3.5 to 20 per cent. However, frequency in total autopsies varies only from 1 to 1.5 per cent. About 70 per cent of aneurysms of the heart are anterior apical in location, about 10 per cent posterolateral, and 20 per cent posterobasal. Anterior apical aneurysms generally show a large bulge measuring 3 to 5 cm in diameter, while posterobasal aneurysms usually measure only 2 to 3 cm in diameter.

Grossly, aneurysms may be *saccular*, but more often they are not sharply demarcated from the ventricular cavity The endocardial surface is frequently the seat of a mural thrombus. The aneurysmal wall proper is thinner than the ventricle prior to infarction, usually adhesions to the overlying epi- and pericardium serve to protect against rupture. Microscopically, the muscle fibers are decreased in size and number, and there are various degrees of necrosis, fibrosis, and hyalinization, depending on the age of the infarct. Calcium deposits are often found in the aneurysm wall

Rupture of a cardiac aneurysm is rare, particularly those consisting primarily of fibrous scar tissue. Almost always, when it occurs, it is in a fresh infarct. Mural thrombus formation in an aneurysm is, however, common.

Causes other than myocardial infarction are rare, although aneurysms have been reported following necrosis of the myocardium in rheumatic fever, gumma of syphilis, endocarditis with myocardial abscess formation, particularly in association with mycotic coronary arteritis, as well as in congenital defects, or due to trauma.

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rhage, hemoconcentration, and hypertension or hypotension (depending upon the intensity of the stress) during the alarm reaction of the "*general adaptation syndrome*" (*Selye et al.*). In addition, it has also been demonstrated that significant changes in hemodynamics and electrocardiographic patterns occur during psychiatric interviews relating to stressful life situations (Stevenson et al.).

Exercise and emotional stress have also been shown to cause, not only changes in blood pressure, but also an increase in blood viscosity and hematocrit and a decrease in sedimentation rate and coagulation and prothrombin times (Schneider, 1951). It would appear, therefore, that there is objective evidence of the influence of physical and emotional factors on the vascular tone and the clotting mechanisms of the blood and that both the central nervous system and the endocrine system may be involved.

PREDISPOSING AND CONTRIBUTING FACTORS

Etiology. It has been suggested that the incidence of coronary artery disease has increased in recent years. *Constitutional factors* are important in coronary artery disease, but there is also evidence of variation of its incidence with *environment*. In addition, its relationship to physical effort is highly controversial. Some maintain that the pain of coronary insufficiency[2] is almost always precipitated by stress, either physical or psychologic, and that these factors are related to coronary insufficiency in roughly 50 per cent of cases but are coincidental in the pathogenesis of coronary thrombosis (Parkinson et al., 1928, Luten, Master et al., 1937). Others believe that sudden, exceptionally heavy physical exertion may be followed by coronary occlusion (Fitzhugh et al., Boas, 1941). In addition, there are those who believe that acute psychologic disturbances may have a direct bearing on coronary occlusion (Arlow, Weiss et al.). All are agreed, however, that preexisting intrinsic coronary artery disease must be present.

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Blumgart has best defined these general factors as three groups: (1) primary etiologic factors which set the stage for the appearance of coronary artery disease, (2) secondary predisposing influences which favor the development of the primary etiologic factors, and (3) immediate precipitating factors.

PRIMARY ETIOLOGIC FACTORS IN THE PRODUCTION OF CORONARY ARTERY DISEASE. At least 90 per cent of cases of myocardial ischemia are due to coronary sclerosis or its sequelae. Uncomplicated and progressive coronary atherosclerosis, resulting from the simple deposition of lipid materials over long periods, is not the common immediate cause of coronary artery disease (Paterson, 1952a). It is well known to pathologists that severe grades of coronary atherosclerosis are not incompatible with good health and normal heart action, while lesser grades of disease may be associated with occlusive phenomena. The studies of Blumgart and Schlesinger have shown that the gradual reduction of the coronary lumen to a pin-point size does not necessarily result in symptoms since it may be compensated for by the opening up of a *collateral circulation*, which is adequate for the ordinary activities of life. If these ordinary activities are exceeded, attacks of precordial pain may occur, due to *acute coronary insufficiency*. This, however, is not the usual way in which coronary artery disease is produced. On the contrary, it is usually precipitated by structural changes in atherosclerotic plaques, changes which have no apparent relation to lipid metabolism at the time of the catastrophe, but are more concerned with extraneous factors, such as coronary pressure, coronary flow, and capillary fragility. Thus, the difference between an individual with clinically evident coronary artery disease and a so-called normal individual lies not so much in his grade of coronary atherosclerosis as in the presence of these extraneous factors which precipitate occlusion. These factors and the occlusive lesions which result may be classified as sequelae to the formation of coronary sclerosis.

Intimal hemorrhage cannot be accepted as a causative lesion in atherosclerosis (because the intima of normal human arteries is not

or peripheral atherosclerosis. Evidence was presented to suggest a possible general association with high fat consumption, but they stated that it was difficult to disentangle this from caloric balance, exercise, changes in body weight, and other metabolic and dietary factors that may be involved. Thus, their review of the evidence at present did not convey any specific implications for drastic dietary changes, specifically in the quantity or type of fat in the diet of the general population, on the premise that such changes would definitely lessen the incidence of coronary or cerebral artery disease. On the other hand, they pointed out the fact that *obesity* is a nutritional failure, that it is caused by consuming more energy than one expends, that diatary fats are the most concentrated source of energy, providing some 40 to 45 per cent of the daily caloric intake, and suggested that many should consume less calories. For most, this would mean eating less fat

In further detail, this Committee emphasized that prudence, as well as habit and taste, would dictate the selection of a diet with some fat Diets providing 25 to 30 per cent of the calories from fat, rather than the current 40 to 45 per cent in the American diet, could still provide palatable meals for our accustomed tastes They concluded that the key points of nutritional common sense for better health generally, and most likely in regard to atherosclerosis specifically, consist of a balanced varied diet that adjusts total calories to reach or maintain a desirable weight [4] Such a diet should provide more protein from lean meat, fish, poultry, and animal products, cereal and grain products, and a reasonable selection of fruits and vegetables The fat content should be sufficient only to meet caloric and essential fatty acid demands They emphasized that these conclusions obviously apply to the general population and not to patients or to individuals with a strong family history of early deaths from cardiovascular disease who are being observed with some regularity by their physician. There the newer concepts of nutrition readily suggest various types of diet therapy that may prove useful to certain patients

Excessive *emotional stress* has been recognized in promoting the appearance of cardiac pain. Sprague reported that some investigators are proposing the view that emotional stress may be the agent through which lipids appear in coronary vessels and thus offer an explanation as to why coronary disease is increasing in what is supposed to be an unusually anxious age in world history Emotional stress has been claimed to result in an increase in serum cholesterol (Rosenman et al.). Miles and coworkers reported the occurrence of anxiety and its possible effects of increased heart rate and output, rise in blood pressure, shortened clotting time, and increased blood viscosity but stated that they did not have evidence that anxiety or other emotional stress is related to the genesis of the atherosclerosis. Sprague summarized that it seems likely that emotional tension results in compulsive eating, drinking, and smoking in many individuals as compensation for anxiety, and he believes that it is through this indirect mechanism that stress has its influence on coronary disease. In addition, he offers the suggestion that emotional stress contributes to the failure to achieve daily physical exercise by promoting fatigue and by forcing a man to make so many commitments that no time is found even for elementary exercise, such as walking.

IMMEDIATE PRECIPITATING FACTORS. There are factors which temporarily increase cardiac work out of proportion to the quantity of blood supplying the myocardium and those which result in a decrease in coronary blood flow.

It is clinically recognized that the "three E's" are frequent causes as immediate precipitating factors in the production of cardiac pain exertion, emotion, and eating.

Physical exercise is the most frequent immediate precipitating cause of cardiac pain. Patients with coronary artery disease subjectively note the occurrence of retrosternal discomfort associated with exertion, but the degree of activity and type of exertion may vary. Cardiac pain may occur after walking one to three blocks on level terrain, while climbing a slight grade may immediately precipitate discomfort. The patient's exercise tolerance is frequently less if he walks rapidly than if he walks at a leisurely pace. In occasional patients, specific physical activity, such as bending over to make beds or raising the arms to hang clothes on a line, causes discomfort. In other patients, the history is obtained that cardiac pain occurs frequently with mild or moderate physical exertion during the early portion of the day and then diminishes in frequency as the patient maintains his activity pattern during the day In many patients, the degree of

[4] See also Part 19, Chaps 4 and 5 *Editor*

rhage, hemoconcentration, and hypertension or hypotension (depending upon the intensity of the stress) during the alarm reaction of the "general adaptation syndrome" (Selye et al.). In addition, it has also been demonstrated that significant changes in hemodynamics and electrocardiographic patterns occur during psychiatric interviews relating to stressful life situations (Stevenson et al.).

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develop a *myocardial infarct.*[a] They either recover from this episode, or death may result from ventricular fibrillation, shock, cardiac decompensation, or myocardial rupture.

The onset of acute *coronary occlusion* is characterized by the abrupt appearance of *severe persistent pain* It is variously described as crushing, choking, sharp, viselike, or agonizing It may assume the form of heaviness, oppression, constriction, or pressure It may be excruciating at the onset, or it may initially be mild, then progressing in severity. An occasional patient may note a disturbed sense of well-being for some hours characterized by gas, indigestion, belching, and fullness prior to the actual acute onset The *precordial pain is characteristically* retrosternal or substernal It may radiate to both arms, the shoulders, neck, throat, and the epigastrium The pain usually lasts one-half hour to several hours It usually does not subside completely without the benefit of medication A dull ache, heaviness, hyperesthesia, or anterior *chest tenderness* usually persists The patient is frequently *nauseated,* and *emesis* may occur The onset of the attack is accompanied by *fear of impending death* The patient is apprehensive, restless, dyspneic, pale or cyanotic, and sweating profusely

Physical examination reveals a cold clammy skin. The pulse may be unobtainable, rapid and poorly sustained, or irregular Blood pressure may be low at shock levels or unobtainable The heart sounds may be muffled or distant, and a triple rhythm (gallop rhythm) is noted frequently Moist inspiratory rales may be present over the lung fields, or acute pulmonary edema (characterized by inspiratory and expiratory rales and rhonchi) may be a manifestation A *pericardial friction rub* may be noted about the second or third day following the acute onset; although generally transient, it may persist for a day to a week.

The appearance of fever, leucocytosis, or an elevated sedimentation rate may occur from the first to the fourth day. The patient's temperature may be subnormal, normal, or elevated. Usually fever does not exceed 101°F; however, the magnitude is roughly proportional to the extent and severity of the myocardial infarct. A leucocytosis in the range of 12,000 to 15,000 cells per cubic millimeter occurs. As with fever, a more marked leucocytosis may occur in more extensive infarcts. The magnitude and duration of fever and leucocytosis may also be influenced by complications, such as infections or pulmonary infarction. Serum glutamic oxaloacetic transaminase (SGO-T), serum lactic dehydrogenase (SLD), and serum glutamic pyruvic transaminase (SGP-T) activity rises within 12 hr and persists for as long as 6 days after acute transmural myocardial infarction.[1] The height and duration of elevation are roughly proportional to the size of the infarction. Cardiac pain per se is not associated with a rise in activity unless presumably accompanied by heart muscle cell damage (LaDue).

The *erythrocyte sedimentation rate* rises within 12 to 24 hr after acute myocardial infarction and may remain elevated for as long as 7 weeks. Unfortunately, this modality may also become abnormal with coronary insufficiency without infarction *C-reactive protein* is also positive in nearly 100 per cent of patients after the third day of acute myocardial infarction and remains elevated for as long as 3 to 7 weeks *Blood fibrinogen level* reacts similarly to C-reactive protein. The ECG is of the utmost importance in establishing a diagnosis of acute myocardial infarction

Beck (1958) has shown that stenosis or occlusion carries two distinct sequelae One concerns differences in oxygen content of muscle and the other concerns inadequate inflow of blood. Differences in oxygenation of muscle produce electric instability, pain, and currents that may be strong enough to cause the heart to fibrillate and result in death of the patient Reduction of inflow produces death of muscle and infarction. Beck emphasizes that, if coronary flow is reduced uniformly, the heart does not fibrillate nor does it produce

[a] An exception is represented by the cases, rather rare in this age group, who develop an occlusion without infarct on account of well-developed collateral circulation Symptoms may then be brief or even absent On the other hand, cases with narrowing of a coronary artery may develop an infarct if there is prolonged and severe coronary insufficiency due to arterial pressure drop, anemia, or excessive blood demand by the myocardium (effort) In such cases, the clinical picture is usually identical with that of coronary occlusion. Editor

[1] See Chap. 4. *Editor.*

in the families of the coronary heart disease group than in those of the control group. Their observations revealed that 9.8 per cent, 37.1 per cent, and 8 6 per cent of the mothers, fathers, and siblings, respectively, of the coronary heart disease patients died from coronary heart disease, in contrast to 7.7 per cent, 18.5 per cent, and 1.0 per cent, respectively, of the mothers, fathers, and siblings of the control group

The strong influence of *heredity* on coronary artery disease cannot be denied, but the mode of gene transference or inheritance and the degree of penetrance have not been clarified by their study.

The incidence of coronary artery disease is increased in individuals with arterial hypertension, diabetes mellitus, obesity, polycythemia vera, thromboangiitis obliterans, periarteritis nodosa, familial xanthomatosis with hypercholesterolemia, essential hyperlipemia, myxedema, and chronic gluomerulonephritis. However, the frequency of coronary lesions in the absence of these diseases suggests that their role in the development of atherosclerosis is not primary but rather that of an aggravating or accelerating factor Thyrotoxicosis, anemia, and tachycardia occurring in the coronary disease age group may precipitate chest pain. Chronic cholecystitis and cholelithiasis, duodenal ulcer, diaphragmatic hernia, and organic and functional disturbances of the esophagus have been documented as aggravating factors in patients with coronary artery disease, but it has not been documented whether they have any direct etiologic influence on the development of atherosclerosis.

The various studies of American and British investigators, classified by a few simple facts on their *smoking habits,* have produced such discrepant findings that, at the least, the existence of any direct relationship between smoking and coronary artery disease of middle age becomes problematic An individual patient with coronary artery disease may exhibit a sensitivity to smoking characterized by tachycardia, palpitation, tremor, and the occurrence of chest discomfort, in such a patient, smoking obviously plays a role in the precipitation of symptoms. The patient's smoking habits as gaged by his daily cigarette consumption may afford a rough index of his emotional response to his daily activity pattern.

The question of *masculinity* in coronary artery disease has been considered at great length. The "robust young male" described by White has been delineated as a male whose physical structure is that of an endomorphic mesomorph: a heavily built, bony, muscular, and sturdy male. Gertler and White observed that the young coronary heart disease patient appeared "one decade older" and offered the explanation that this may be due in part to the normal "older appearance" of mesomorphy. The coronary patient has further been described as being a hard-driving, goal-directed, meticulous individual whose monodirective personality suggests refuge in work. The investigation of the relation of *athletics* to coronary heart disease yielded interesting information. The coronary group in Gertler and White's series scored higher in their athletic ratings than did comparable controls. This fact might well be attributed to mesomorphy.

Coronary heart disease is said to be uncommon among the Chinese, Japanese, Okinawans, and Bantu tribesmen in South Africa (Keys et al., 1955).[3] Ethnic origin as an original factor in coronary heart disease was also considered in Gertler and White's study. The predominance of Jews in their series was in keeping with the observations of other investigators; the reason for it, however, is not clear It is known that Jews are particularly prone to diseases involving abnormal lipid metabolism, such as Tay-Sachs disease, Gaucher's disease, and Niemann-Pick disease They offered the suggestion that this high incidence may in part be due to the high degree of endogamy in Jews.

It has been suggested that the *nutritional status* of an individual is an important environmental factor in the etiology of atherosclerosis (Page et al).

In a report to the American Heart Association, the Nutrition Committee summarized and evaluated evidence for and against the concept that the *fat content* of the average present-day North American or north European diet is a significant factor in the genesis of cerebral, myocardial, renal,

[3] See also Part 5, Chap. 3 *Editor.*

develop a *myocardial infarct.*[6] They either recover from this episode, or death may result from ventricular fibrillation, *shock*, cardiac decompensation, or myocardial rupture

The onset of acute coronary occlusion is characterized by the abrupt appearance of *severe persistent pain* It is variously described as crushing, choking, sharp, viselike, or agonizing It may assume the form of heaviness, oppression, constriction, or pressure. It may be excruciating at the onset, or it may initially be mild, then progressing in severity. An occasional patient may note a disturbed sense of well-being for some hours characterized by gas, indigestion, belching, and fullness prior to the actual acute onset The *precordial pain* is characteristically retrosternal or substernal. It may radiate to both arms, the shoulders, neck, throat, and the epigastrium. The pain usually lasts one-half hour to several hours It usually does not subside completely without the benefit of medication. A dull ache, heaviness, hyperesthesia, or anterior chest tenderness usually persists. The patient is frequently *nauseated*, and *emesis* may occur. The onset of the attack is accompanied by fear of impending death The patient is apprehensive, restless, dyspneic, pale or cyanotic, and sweating profusely

Physical examination reveals a cold clammy skin The pulse may be unobtainable, rapid and poorly sustained, or irregular Blood pressure may be low at shock levels or unobtainable The heart sounds may be muffled or distant, and a triple rhythm (gallop rhythm) is noted frequently Moist inspiratory rales may be present over the lung fields, or acute pulmonary edema (characterized by inspiratory and expiratory rales and rhonchi) may be a manifestation A *pericardial friction rub* may be noted about the second or third day following the acute onset; although generally transient, it may persist for a day to a week.

The appearance of fever, leucocytosis, or an elevated sedimentation rate may occur from the first to the fourth day. The patient's temperature may be subnormal, normal, or elevated. Usually fever does not exceed 101°F; however, the magnitude is roughly proportional to the extent and severity of the myocardial infarct. A leucocytosis in the range of 12,000 to 15,000 cells per cubic millimeter occurs. As with fever, a more marked leucocytosis may occur in more extensive infarcts. The magnitude and duration of fever and leucocytosis may also be influenced by complications, such as infections or pulmonary infarction. Serum glutamic oxaloacetic transaminase (SGO-T), serum lactic dehydrogenase (SLD), and serum glutamic pyruvic transaminase (SGP-T) activity rises within 12 hr and persists for as long as 6 days after acute transmural *myocardial infarction.*[7] The height and duration of elevation are roughly proportional to the size of the infarction. Cardiac pain per se is not associated with a rise in activity unless presumably accompanied by heart muscle cell damage (LaDue).

The *erythrocyte sedimentation rate* rises within 12 to 24 hr after acute myocardial infarction and may remain elevated for as long as 7 weeks. Unfortunately, this modality may also become abnormal with coronary insufficiency without infarction *C-reactive protein* is also positive in nearly 100 per cent of patients after the third day of acute myocardial infarction and remains elevated for as long as 3 to 7 weeks. *Blood fibrinogen level* reacts similarly to C-reactive protein. The ECG is of the utmost importance in establishing a diagnosis of acute myocardial infarction.

Beck (1958) has shown that stenosis or occlusion carries two distinct sequelae One concerns differences in oxygen content of muscle and the other concerns inadequate inflow of blood. Differences in oxygenation of muscle produce electric instability, pain, and currents that may be strong enough to cause the heart to *fibrillate* and result in death of the patient Reduction of inflow produces death of muscle and infarction. Beck emphasizes that, if coronary flow is reduced uniformly, the heart does *not* fibrillate nor does it produce

[6] An exception is represented by the cases, rather rare in this age group, who develop an occlusion without infarct on account of well-developed collateral circulation Symptoms may then be brief or even absent On the other hand, cases with narrowing of a coronary artery may develop an infarct if there is prolonged and severe coronary insufficiency due to arterial pressure drop, anemia, or excessive blood demand by the myocardium (effort) In such cases, the clinical picture is usually identical with that of coronary occlusion *Editor*

[7] See Chap. 4. *Editor.*

in the families of the coronary heart disease group than in those of the control group. Their observations revealed that 9.8 per cent, 37.1 per cent, and 8.6 per cent of the mothers, fathers, and siblings, respectively, of the coronary heart disease patients died from coronary heart disease, in contrast to 7.7 per cent, 18.5 per cent, and 1.0 per cent, respectively, of the mothers, fathers, and siblings of the control group

The strong influence of *heredity* on coronary artery disease cannot be denied, but the mode of gene transference or inheritance and the degree of penetrance have not been clarified by their study.

The incidence of coronary artery disease is increased in individuals with arterial hypertension, diabetes mellitus, obesity, polycythemia vera, thromboangiitis obliterans, periarteritis nodosa, familial xanthomatosis with hypercholesterolemia, essential hyperlipemia, myxedema, and chronic gluomerulonephritis. However, the frequency of coronary lesions in the absence of these diseases suggests that their role in the development of atherosclerosis is not primary but rather that of an aggravating or accelerating factor. Thyrotoxicosis, anemia, and tachycardia occurring in the coronary disease age group may precipitate chest pain. Chronic cholecystitis and cholelithiasis, duodenal ulcer, diaphragmatic hernia, and organic and functional disturbances of the esophagus have been documented as aggravating factors in patients with coronary artery disease, but it has not been documented whether they have any direct etiologic influence on the development of atherosclerosis.

The various studies of American and British investigators, classified by a few simple facts on their *smoking habits*, have produced such discrepant findings that, at the least, the existence of any direct relationship between smoking and coronary artery disease of middle age becomes problematic An individual patient with coronary artery disease may exhibit a sensitivity to smoking characterized by tachycardia, palpitation, tremor, and the occurrence of chest discomfort; in such a patient, smoking obviously plays a role in the precipitation of symptoms. The patient's smoking habits as gaged by his daily cigarette consumption may afford a rough index of his emotional response to his daily activity pattern.

The question of *masculinity* in coronary artery disease has been considered at great length. The "robust young male" described by White has been delineated as a male whose physical structure is that of an endomorphic mesomorph: a heavily built, bony, muscular, and sturdy male. Gertler and White observed that the young coronary heart disease patient appeared "one decade older" and offered the explanation that this may be due in part to the normal "older appearance" of mesomorphy. The coronary patient has further been described as being a hard-driving, goal-directed, meticulous individual whose monodirective personality suggests refuge in work. The investigation of the relation of *athletics* to coronary heart disease yielded interesting information. The coronary group in Gertler and White's series scored higher in their athletic ratings than did comparable controls This fact might well be attributed to mesomorphy.

Coronary heart disease is said to be uncommon among the Chinese, Japanese, Okinawans, and Bantu tribesmen in South Africa (Keys et al., 1955).[3] Ethnic origin as an original factor in coronary heart disease was also considered in Gertler and White's study. The predominance of Jews in their series was in keeping with the observations of other investigators, the reason for it, however, is not clear. It is known that Jews are particularly prone to diseases involving abnormal lipid metabolism, such as Tay-Sachs disease, Gaucher's disease, and Niemann-Pick disease. They offered the suggestion that this high incidence may in part be due to the high degree of endogamy in Jews.

It has been suggested that the *nutritional status* of an individual is an important environmental factor in the etiology of atherosclerosis (Page et al.).

In a report to the American Heart Association, the Nutrition Committee summarized and evaluated evidence for and against the concept that the *fat content* of the average present-day North American or north European diet is a significant factor in the genesis of cerebral, myocardial, renal,

[3] See also Part 5, Chap. 3. *Editor.*

examination may reveal retinal arteriolar sclerosis out of proportion to the patient's chronological age group, or the eyegrounds may be normal. The heart size is invariably normal, at least during the early stage of the disease. There may be no murmurs, triple rhythm (gallop rhythm), or arrhythmia. The heart sounds are usually normal, or the aortic 2d sound may be *accentuated* The latter must be considered in terms of the patient's chronological age, in so far as being an abnormal finding is concerned The peripheral arterial pulses may be normal, or they may be diminished in the lower extremities. This finding, if present, is a reflection of the diffuse involvement of the vascular system by the atherosclerotic process Blood sugar and serum cholesterol may be abnormal or elevated. Chest x-ray or fluoroscopy may reveal the heart size to be normal. The great vessels may appear normal, or the aorta may be increased in density and tortuous. The ECG pattern may be entirely normal or reveal only generalized decrease in amplitude of the T waves.

Between the ages of 50 and 59, the male-to-female ratio may approximate 10.1 in this group, while after the age of 70, it becomes less than 2.1 (Peel)

The clinical course in this group of patients may vary both in rate of progression and the terminal event As indicated, some of these patients may eventually suffer a coronary occlusion. Others may continue to note symptoms of myocardial ischemia, the cardiac pain may initially occur frequently and then improve or subside, or it may exhibit cyclic variations of exacerbation and remission, or it may gradually progress both in frequency and severity In these cases, the extensive replacement of myocardium by fibrous tissue may eventually produce a syndrome of *intractable heart failure*

It is important to recognize that blood supply is deficient only in relation to the requirements of the myocardium to accomplish its work The coronary blood flow may be adequate to meet the normal myocardial needs at rest but insufficient for the increased requirements when the work of the heart is increased, as in exercise, emotion, eating, walking against a cold wind, or rises in blood pressure The pathologic basis for this discrepancy between supply and demand is revealed by the striking prevalence of arteriosclerotic coronary narrowings and occlusions in patients with cardiac pain. Ninety per cent of the hearts of patients with cardiac pain studied by Blumgart et al. (1940) have shown obstructive narrowings and occlusions of the main coronary arteries or their primary branches Similar lesions were occasionally found in the hearts of patients who had no cardiac symptoms during life and who died of noncardiac causes, but the incidence and severity of such lesions were strikingly less. This apparent inconsistency between the presence of long-standing obstructive arterial lesions and the absence of pathologic or clinical evidence of myocardial infarction was explained by the demonstration of *collateral channels* which by-passed the obstructions or which supplied the myocardium distal to the areas of narrowing or occlusion from neighboring unoccluded coronary arteries[6]

Every heart with chronic occlusion has intercoronary channels This fact is open to two interpretations either occlusion produced them, or they were always present because they were essential About 9 per cent of persons are born with *well-developed intercoronary channels* Their heart is in a favorable position to continue to beat as the stenosing disease increases, and if it can go through the crisis of occlusion, then an excellent set of intercoronaries develops. Occlusion seems to be an excellent stimulus for intercoronaries, provided that those patients who fell by the wayside as the stenosing process became more severe are not taken into consideration (Beck, 1958) The patient with clinical evidence of coronary heart disease has a precariously balanced circulation in which small alterations may produce important consequences.

Group 3: Mild or Subclinical Coronary Heart Disease. The third group comprises those patients who have minimal symptoms and minimal disability. Their physical and laboratory findings are entirely normal These patients may become relatively asymptomatic following the initial onset of symptoms. Others may note mild discomfort intermittently, but their clinical course is characterized by no disability However, in this group of patients,

[6] See Chaps 8, 9, and 10 and also Part 1, Chap. 6 *Editor.*

exercise tolerance is remarkably constant. Walking in cold weather commonly influences the occurrence of cardiac pain. In volunteering this cause for their chest discomfort, these patients frequently add that during the cold-weather period when walking outdoors they place a handkerchief or scarf over their nose. Walking against the wind during the winter season causes chest pain.

Patients with coronary heart disease often note the occurrence of symptoms *after eating*. Close questioning frequently reveals that the cardiac pain does not occur so much immediately after the act of ingesting a meal as it does when the patient gets up and walks away from the table or performs some physical activity following eating. This suggests that a smaller degree of physical work is required to precipitate cardiac pain immediately following ingestion of a meal Patients with disease of the gastrointestinal system (gallbladder disorders, peptic ulcer, esophageal hiatus hernia, esophageal spasm) frequently note the precipitation of cardiac pain following the ingestion of a heavy meal Kuo and Joyner have reported precipitating cardiac pain in patients with coronary disease by the feeding of a high-fat meal.

Emotional stress is a common immediate precipitating factor of cardiac pain. This factor may be difficult to evaluate in a particular patient because (1) emotional stress may precipitate cardiac pain, (2) patients with coronary artery disease most often exhibit a significant degree of emotional overlay; and (3) patients with primary neurocirculatory asthenia may experience symptoms analogous to those observed in coronary artery disease [5] This difficulty in evaluating the symptoms of chest discomfort in an emotionally unstable patient becomes all the more complex when it is recognized that the patient's history may represent the *only positive finding* in coronary heart disease The precipitation of the discomfort upon effort, the characteristic location of the pain or oppression behind the sternum with radiation to the arms, neck, or angle of the jaw, the disappearance of the discomfort upon cessation of effort, and the relief following administration of sublingual nitroglycerin are beneficial in helping to differentiate cardiac pain. Administration of placebos has not proved to be specifically useful in the differentiation of chest discomfort in emotionally unstable individuals because of the role of suggestion in this group of patients and because placebos themselves are recognized as being capable of inducing subjective symptoms. Thus, in the individual experiencing chest discomfort and exhibiting profound emotional instability, the diagnosis of coronary artery disease may be difficult in the absence of other objective evidence. However, in the patient with an established clinical impression of coronary artery disease, it is well recognized that emotional stress frequently precipitates symptoms. This is verified by the symptomatic improvement in many of these patients when the factors contributing to emotional instability are controlled.

The occurrence of *severe tachycardia* or *hypertension* may precipitate cardiac pain A reduction in coronary blood flow (such as may occur in hypotension and shock), reduced circulating blood volume, severe bradycardia, and hypotension may result in cardiac pain, especially in dehydrated or hypoglycemic patients.

Occasionally *tobacco* precipitates paroxysms in susceptible individuals. Epinephrine, insulin, thyroid extract, and Pitressin are drugs which may cause cardiac pain.

In some patients, cardiac pain is precipitated by assuming the recumbent position, especially at night. The latter may be confused with the symptoms associated with the occurrence of orthopnea, paroxysmal nocturnal dyspnea, or acute myocardial infarction.

CLINICAL SYNDROMES CAUSED BY CORONARY ARTERY DISEASE

The history of coronary artery disease may vary from one individual to another, but the clinical course of the majority of patients may be classified into the following three groups.

Group 1: Coronary Occlusion. Myocardial Infarct. This group includes patients in the 35- to 55-year-old age group who are in excellent health, without a previous history of symptoms or signs of coronary artery disease. Their clinical course is characterized by the *sudden occurrence of a coronary occlusion*. They usually

[5] See Part 17, Chap 2 *Editor*.

The pain is characteristically of brief duration, lasting a matter of only a few minutes. It may be severe at the onset, or it may begin in a mild form and quickly increase in severity as the precipitating factor is maintained In the majority of cases, the precipitating factor is *exercise* During the period of pain, the patient's sense of well-being is markedly disturbed, and depending upon the severity and duration, he may experience a feeling of suffocation, inability to breathe, or a *sense of impending death*[10]

When in public places, the patient often attempts to divert attention from himself by gazing into a store window or appearing to be occupied in inspecting some object. In the majority of cases, the precipitating factor is exercise, and when effort is discontinued, cardiac pain is promptly relieved unless an infarction has occurred Emotional stress and eating are also frequent precipitating factors, but even in these cases, the precipitation of cardiac pain by effort is a common finding The relief of the chest discomfort by nitrites is of prime importance in the evaluation Usually *sublingual nitroglycerin* induces prompt relief[11] If it does not, it may be because the chest discomfort is *not* due to myocardial ischemia, or the pain is associated with an impending or actual myocardial infarction, or the dose is not sufficient On the other hand, nitroglycerin tablets may be aged and not dissolve rapidly under the tongue The use of placebos in the evaluation of cardiac pain may be potentially hazardous in those individuals with more severe symptoms due to myocardial ischemia Nitroglycerin sublingually also offers relief when taken prophylactically, just before the pain is likely to occur This may be particularly useful in the evaluation of those patients whose pain occurs regularly under similar circumstances

Functional Tests Various tests have been devised for the study of patients in whom the diagnosis of coronary heart disease remains uncertain. These tests are based upon the principle that myocardial ischemia will simultaneously produce pain and electrocardiographic changes. The stimulus to precipitate cardiac pain and simultaneously monitor electrocardiographic changes is brought about by the *anoxemia test* or the *exercise test*.

The *anoxemia test* is performed by having the patient breathe a mixture of 10 per cent oxygen and 90 per cent nitrogen for varying intervals, usually for 20 min, unless cardiac pain is precipitated earlier (Levy et al, 1941). One hundred per cent oxygen is available in case the patient experiences significant discomfort which does not subside immediately upon inhalation of room air. A control ECG is obtained prior to the test and at 5-min intervals during the low-oxygen inhalation. If abnormalities appear, serial ECG patterns continue to be recorded until the changes revert to the control pattern Since there is no specific information as to the degree of arterial unsaturation produced in any individual patient during the period of inhalation, it has been suggested that an ear oximeter be utilized and that the oxygen saturation should be maintained at 70 to 75 per cent (Turner et al; Penneys). The test is termed positive and the diagnosis of coronary artery disease is supported if pain occurs during the low-oxygen inhalation or if certain electrocardiographic abnormalities are noted There is no uniform agreement as to the criteria for evaluation of the RS-T-segment and T-wave changes Burchell and associates found that the precordial leads were more informative than the standard leads and could be used exclusively if desired. A negative test does not exclude the presence of coronary artery disease

The *exercise test* has undergone many modifications, but the two-step exercise ECG test as described by Master involves the performance within 1½ min of usually 15 to 25 trips up and down two steps, each 9 in high Published tables vary the number of trips with age, weight, and sex of the patient If the *single two-step test* is normal, the *double two-step test* may be applied This involves *twice* as many trips within a time limit of 3 min A control ECG is obtained utilizing leads II, V_3, V_4, and V_5. The postexercise ECG is obtained as rapidly as possible, and tracings are repeated until any changes which might have occurred revert to normal. The essential criterion of a positive two-step test is an RS-T-segment depression of more than 0 5 mm below the isoelectric level.

Both the anoxemia test and the exercise test are potentially hazardous, and the individual

[10] This fearful sensation was considered typical of "angina pectoris" for over a half century Actually, few patients with coronary disease complain of it unless they have suffered from a coronary occlusion *Editor*

[11] The physician *should* be aware that nitroglycerin may dilate smooth muscles of various organs including bronchi, gallbladder, etc Thus, various forms of "noncoronary" pain may be relieved by it. *Editor*

pain. According to Beck's thesis, there are various types of death produced by coronary artery disease. One is due to the fibrillating currents that destroy the heart beat, this is the fatal heart attack. The other is due either to inadequate inflow of blood or to muscle destruction: the heart goes into failure or it simply stops beating (standstill). A third possibility would occur in the absence of severe muscle damage and when there is no severe inflow reduction and no fibrillation: the heart would fail to convert its energy substances into mechanical energy.

It should be mentioned that in the coronary syndrome being described variations in severity may occur.

Prinzmetal described the typical patient with a "mild" myocardial infarction as being young or middle-aged He is usually vigorous, active, and apparently in excellent health. He has never had a previous myocardial infarct or any other clinically evident heart disease. There has been no hypertension, diabetes, or other significant chronic illness. The pain associated with the infarction is of relatively short duration. It usually responds readily to medication and does not recur. Shock is not present Temperature elevation following the attack is absent, minimal, or of short duration. Leucocytosis is mild and the erythrocyte sedimentation rate only slightly increased Serum transaminase levels are only moderately elevated. The heart does not become enlarged, triple rhythm (gallop rhythm) does not occur, and signs of congestive failure do not appear at any time during the course of the illness Significant arrhythmias are not observed. Within a day or two after the onset, the patient looks and feels well Unless he has been seriously frightened by the attack, he is usually eager to get up and return to work It is likely that an occasional patient in this category will diet within 2 weeks after the onset as a result of an extension of the originally small infarct or will develop a new infarct soon after the first. Death may also occasionally result from an otherwise "mild" infarction which involves the AV node causing Stokes-Adams attacks or from arrhythmias Prinzmetal concluded that these "mild" cases have an extremely low immediate mortality, certainly less than 1 per cent

It has been estimated by Wright et al that nearly a million myocardial infarctions occur every year in the United States Prinzmetal suggests that modern techniques make it possible to classify most cases of acute myocardial infarction into three categories: mild, moderate, and severe. Some cases are unclassifiable since there is no sharp line of demarcation between these groups. All other things being equal, it would appear that the severity of the clinical picture in acute myocardial infarction is largely dependent upon the amount of tissue necrosis.

If a very few grams, or less, of myocardium become necrotic following thrombosis of a small coronary artery branch in a young, otherwise healthy, individual, the clinical manifestations are apt to be mild and may even be overlooked completely; the mortality is usually less than 1 per cent. On the other hand, if most or all of the left ventricle, involving perhaps 200 Gm of myocardium, becomes infarcted after closure of a large coronary artery, the mortality will be virtually 100 per cent.

It should be remembered, however, that an originally mild case may become severe as a result of extension of the infarct or the occurrence of a new infarction Any attempt to classify the degree of acute infarction in no way implies that even a very small acute myocardial infarction is not of great importance. However, the immediate mortality rate in mild cases must be extremely low and certainly much lower than the average of all myocardial infarctions.

Group 2: Recurrent Episodes of Coronary Insufficiency. In this group of patients, sudden substernal or precordial pain is initiated by effort, emotional stress, or eating. It may vary in severity from simply being annoying to actually compelling the patient to stop his activity, but it is *usually of short duration*. The frequency of the precordial pain may increase over a variable period of time, resulting in significant disability to the patient. In some patients, this clinical course is interrupted by the occurrence of an acute coronary occlusion In others, the precordial-pain pattern and precipitating factors remain remarkably constant or may exhibit exacerbations and remissions without the occurrence of infarction. In these patients, the history of retrosternal pain or oppression following the known precipitating factors may be the only positive feature of the disease.

The physical examination, as well as the laboratory studies, may be entirely normal. On the other hand, the patient may be obese and present physical or laboratory evidence of hypertension or diabetes. The funduscopic

quent. A leucocytosis develops within a few hours following infarction, reaching a maximum of 12,000 to 15,000 and then declining within 1 week.

Laboratory Aids. Serum glutamic oxaloacetic transaminase (SGO-T) is a specific tissue enzyme present in normal heart muscle. Acute transmural myocardial infarction is followed by an increase in the activity of this enzyme in the serum (normal value 22.1 ± 6 units, 24 hr postinfarction 50 to 600 units) (LaDue).[13] Since the activity of this enzyme is 5,000 to 10,000 times greater in heart muscle than serum, that of lactic dehydrogenase (LD) 3,000 greater, and that of glutamic pyruvic transaminase (GP-T) 1,000 times greater, release of these enzymes from damaged cells probably accounts for the increase in serum activity following acute myocardial infarction. There is no consistent relationship between the SGO-T activity and the erythrocyte sedimentation rate, the white blood count, or the C-reactive protein levels.

The SGO-T activity is not increased as a result of infectious, degenerative, neoplastic, allergic, reactive, or congenital diseases or pregnancy unless there is associated acute damage of heart muscle, skeletal muscle, liver, kidney, or brain. The SGO-T activity increases proportionately more than the SLD or SGP-T following acute human myocardial infarction. The SGO-T level has proved particularly useful in deciding whether acute heart muscle cell damage has occurred when chest pain, like that seen with myocardial infarction, develops in patients with equivocal electrocardiographic changes. In such instances, if the SGO-T is carefully followed throughout the duration of pain and for 4 to 12 days afterward, many patients may be saved weeks of invalidism, or on the contrary, anticoagullant therapy may be instituted in order to prevent impending infarction. Acute myocardial damage must be presumed to be present in patients with chest pain and equivocal electrocardiographic changes and who have SGO-T elevation in the absence of known active liver disease. The SGO-T activity will usually help distinguish acute pericarditis and pulmonary infarction from acute myocardial infarction, since SGO-T is uncommonly and only slightly and irregularly elevated following acute pericarditis and pulmonary infarction but rises promptly and follows a characteristic curve after acute myocardial infarction.

The nonspecific phase reactants, including the erythrocyte sedimentation rate, the C-reactive protein, and fibrinogen, have also been evaluated as diagnostic aids in the diagnosis of acute myocardial infarction (Boltax et al.; Volk et al.).

The erythrocyte sedimentation rate becomes elevated within 12 to 24 hr after acute myocardial infarction and may remain elevated for as long as 7 weeks. In almost 100 per cent of patients sustaining an acute transmural myocardial infarction, the C-reactive protein is positive after the third day (Kroop et al., Wallach et al.). The test for C-reactive protein remains positive for as long as 3 to 7 weeks, although it is usually elevated for only 2 weeks in the absence of complications, and returns to normal before the sedimentation rate in most instances. The C-reactive protein is of particular value when blood samples are not obtained within the first four days following myocardial infarction since it remains positive much longer than the SGO-T. The blood fibrinogen level reacts similarly to the C-reactive protein.

All these nonspecific phase reactants (including the sedimentation rate, C-reactive protein, and fibrinogen) are strongly positive following many infectious diseases, neoplastic diseases, gout, some gastrointestinal disorders, pulmonary infarctions, arthritis, and acute rheumatic fever. Therefore, changes in the tests must be carefully evaluated when used as a diagnostic aid for acute myocardial infarction.

X-Ray. X-ray examination of the heart in coronary artery disease may be entirely normal. Following a healed infarct, disturbances in the pulsations of the left ventricle can often be observed by fluoroscopic, roentgenographic, kymographic, or electrokymographic examination.[14] Upon fluoroscopic examination one may observe a localized absence of pulsation along the left ventricle or a localized paradoxic pulsation (systolic expansion) involving a portion of the left ventricle. Occasionally, myocardial infarction may result in myocardial calcification. Complications of coronary artery disease and myocardial infarct may re-

[13] See Chap. 4. *Editor.*

[14] See Chaps. 6 and 7. *Editor.*

emotional stress, work load, and work schedule may build up to a peak; they may experience marked and sustained improvement upon developing an insight into the factors influencing their symptoms. Obesity and an excessive emotional component contribute to some of these patients experiencing continued discomfort. Also occasionally in this group of patients the fear of heart disease influences discomfort and even disability out of proportion to the degree of cardiac pain.

In addition to emotional stress and obesity, the clinician is likely to encounter in this group a number of patients with disease of the biliary and gastrointestinal tract. Chronic cholecystitis and cholelithiasis, duodenal ulcer, diaphragmatic hernia, and organic and functional disturbances of the esophagus have been documented as causes of discomfort. The available evidence suggests that disease of the biliary tract is more common in patients who die of coronary disease than in control groups of patients (Breyfogle). That these individuals have two diseases is supported by the clinical observation that, following surgical removal of the gallbladder in chronic cholecystitis, the symptom of cardiac pain persists and may become more typical. Other extracardiac causes are aortic aneurysm, paroxysmal hypertension, and paroxysmal tachycardia.

A clinicopathologic study of coronary heart disease revealed that, in a series of 30 patients who had recent myocardial infarcts with coronary occlusion, 76 per cent had pain and 24 per cent were asymptomatic. It was further noted that the pain was usually severe when infarction resulted from coronary occlusion, milder if occlusion was not present The investigators emphasized that the *intensity of the ischemia is the important factor in the production of pain, whereas the duration of the ischemia is most important in the production of infarction* (Snow et al). Since infarcts do occur in the absence of pain, it is apparent that group 3 patients may eventually develop such a complication. However, the majority of these patients present a benign course and attain or exceed average life expectancy. Death may result from disease involving systems other than the cardiovascular or may follow a course of gradual, slowly progressive cardiac decompensation secondary to chronic myocardial fibrosis.

DIAGNOSIS

The diagnosis of coronary heart disease is based primarily upon the patient's history and not on objective findings, except in the cases of acute myocardial infarction, where a positive history of cardiac pain is more likely to be associated with significant physical and laboratory findings which document the diagnosis. In patients with the benign form of the disease, a carefully detailed history may reveal the only positive clue to the presence of coronary heart disease.

The clinical history is specific for (1) the substernal or retrosternal site of cardiac pain, (2) the characteristic sites of radiation to the shoulders, arms, neck, throat, or upper abdomen; (3) the precipitation of the pain by effort or emotional stress or after eating; (4) the brief duration; (5) the improvement in the pain upon cessation of effort, or the progression of the pain if effort is continued, (6) the rapid improvement in the pain following the use of nitrites.

The characteristic site of initiation of the symptom of *precordial pain* of cardiac origin is substernal or retrosternal.[9] Many patients find it difficult to describe this symptom. It may vary from a sharp pain to a tight constriction to a sense of heavy oppression over the upper middle anterior chest. Many patients place their hand over the anatomic site to indicate the point of maximal sensation. Pain due to muscle ischemia progresses to impart varied subjective feelings such as tightness, paresthesia, a drawing sensation, cramping, and sharp pain and numbness.

One might obtain an idea of the symptom complex by placing a blood pressure cuff around the arm and impairing the inflow of blood to the extremity This imparts some understanding in regard to the difficulty patients with myocardial ischemia pain experience in describing their symptom The retrosternal pain may radiate to the left shoulder and down the ulnar aspect of the left arm, or it may involve both shoulders and both arms The sites of radiation may skip and involve a portion of the arm or wrist, the neck, throat, or upper abdomen An occasional patient may direct his complaint more to the site of radiation than precordially, but close questioning usually reveals the occurrence of precordial pain of some degree.

[9] See note 2. *Editor.*

ing cove-plane inversion of the T waves; gradual recovery of normal repolarization is marked by progressive decrease in the depth of the inverted T waves and eventual replacement by normal upright T waves. The evolution is usually much slower in infarction than in other types of subepicardial injury.

Preservation of the overlying subepicardial layer in *acute subendocardial infarction* permits registration of the effects of acute subendocardial injury, namely, abnormal sagging or horizontal depression of the S-T junction in *overlying leads*, with progressive changes in serial tracings. Subsidence is manifested by gradual return of the S-T segment to the isoelectric line. Residual delay in repolarization of the subendocardial layer may result in broad upright T waves with prolonged Q-T interval.

When there is an antecedent q wave, notching of the ascending limb of the R is referable to a defect in conduction in the outer wall of the left ventricle and may be correlated with healed patchy infarction at autopsy.

The QRS complex over the area of *subepicardial infarction* commonly shows a reduction in amplitude of the R wave when compared with a tracing taken prior to infarction. The Q-T interval is characteristically above the upper limits of normal; there are changes of the S-T junction, S-T segment, and T wave characterized by elevation, descent to isoelectric line, and depression.

Subepicardial ischemia or *transmural ischemia* results in transient elevation and straightening of the S-T segment with monophasic upright T, followed by rapid return of the S-T junction to the isoelectric line, accompanied by cove-plane inversion of the T wave. The QRS pattern remains normal in serial tracings as long as the ischemic area does not become infarcted, whereas abnormal Q waves appear in the event of extension of the infarct into a previously ischemic area.

Subendocardial ischemia is characterized by a transitory horizontal or downwardly sagging depression of the S-T segment amounting to 0.5 mm or more. Reversal in the direction of the T wave is usually secondary to the primary and significant S-T displacement; changes in the direction of the T wave without alteration in the S-T segment are not diagnostic.

The surface relations of the acutely ischemic area may be roughly mapped out from the leads showing the acute S-T depression; e.g., localization [illegible]
to leads V_4, [illegible]
anterolatera [illegible]
to leads V_7, [illegible]
posterior [illegible]
points to ischemia of the *septum*.

Leads over the opposite intact wall tend to show patterns which are *reciprocal* to those recorded in leads facing the infarct; they present exaggeration of the R wave, initial depression of the S-T junction, and progressive return to the isoelectric line, together with increasing height of the erect T wave.

Estimation of the Size and Location of the Infarct with Reference to the Cardiac Surface. INFARCTION OF THE ANTERIOR WALL OF THE LEFT VENTRICLE. The *large infarct* usually involves the apical third to two-thirds of the anterior wall, continues into the adjoining septum and into the apical third or more of the lateral wall. Large anterior infarcts usually have a central zone of sufficient size to permit the registration of QS patterns in one of three overlying leads, usually V_3, V_4, and V_5. Large anterior infarcts also continue around the tip of the left ventricle into the apical portion of the *posterior* wall. Extensions limited to the apical third of the posterior wall are seldom recognizable in the usual chest and limb leads; extensions into the apical half or *more* of the posterior wall are generally manifested by abnormal QR patterns in lead aVF and in leads from the back below the diaphragm. Patchy infarction or smaller areas of confluent infarctions may not have a sufficiently extensive *marginal* zone to permit the registration of abnormal QR patterns but may, nevertheless, exhibit typical serial S-T-T evolution.

INFARCTION OF THE SEPTUM. This occurs as a part of practically all large anterior *infarcts*, of most posterior infarcts, but not of primary lateral infarcts. Furthermore, the infarct *may* be primary in the *septum* but seldom remains confined to this structure, usually extending into the anterior wall of the left ventricle, less commonly into the posterior wall. The association of *AV block* with signs of posterior (more seldom *anterior*) infarction suggests extension into the septum and AV node. Infarction of the septum *may* not produce QRS abnormalities, particularly after healing, or may be manifested by one of the following patterns.

Right BBB produces a diagnostic QR pattern, characterized by a QRS interval of 0.12 sec or more, an abnormal Q wave, and a prominent late

selection of patients subjected to these tests should be emphasized. Patients with abnormal ECGs should not be submitted to them. Burchell and associates performed 730 hypoxemia tests without a fatality, but occasional unpleasant, and even serious, reactions have been observed (Weintraub et al.). Although the exercise test has potential danger for the patient with serious coronary disease, it is rarely harmful and is usually free of the unpleasant reactions sometimes observed during the anoxemia test. One should not regard these tests as the final determinant in establishing the diagnosis of coronary artery disease but rather as supplemental to the clinical history.

Scarborough and Baker define *ballistocardiography* as measuring mass movements of the body in response to movements in the circulation and, by so doing, giving objective information about the over-all performance of the circulatory system.[12] In this sense, the term mass movements refers to movements, not only of the mass of circulating blood, but also of such masses as the heart itself during the cardiac cycle.

Much of the effort in clinical ballistocardiography has been directed toward an evaluation of patients with coronary artery disease because of the limited value of other objective methods It has been clearly established that the majority of patients with either cardiac pain or a history of myocardial infarction have abnormal ballistocardiograms at rest, and in some of them there is no other objective evidence of cardiovascular disease This would suggest that the method has real clinical value, were it not for the fact that abnormal ballistocardiograms are found in normal individuals above the age of 40 and more and more frequently with increasing age. In the age range below 40, abnormal records from normal subjects are unusual but normal records from patients with coronary artery disease are common. Although it seems fair to assume that many older normal individuals have subclinical coronary artery disease, there is no proof as yet that this is the cause of their frequently abnormal ballistocardiograms At present, these considerations limit the diagnostic value of ballistocardiography in coronary artery disease.

[12] See Part 4, Chap. 4. *Editor*

Clinical Symptoms. The diagnosis of acute myocardial infarction in patients with coronary artery disease is supported by the positive clinical history, together with frequently abnormal objective laboratory studies. These laboratory determinations are important, not only from a diagnostic standpoint but also in following the course of the infarction and its subsequent healing. Coronary occlusion does occur in some patients without pain, whereas in others it is accompanied by cardiac pain of unusually severe degree.

Prodromal pain in coronary occlusion has been described by Blumenthal and Reisinger who conclude that intramural hemorrhage may be an important factor. The clinical picture of acute myocardial infarction may present itself as (1) cardiac pain, (2) shock, (3) acute pulmonary edema, (4) chronic progressive cardiac decompensation (exertional dyspnea, orthopnea, chronic fluid retention), or (5) an acute vascular accident occurring in some other vascular area, such as the brain. In acute myocardial infarction, cardiac pain is usually more severe and of longer duration than in the benign stage of coronary artery disease. It may not respond to sublingual nitroglycerin It may occur at rest, as well as after exercise. The pain may last for several hours or days. In other cases, pain is of short duration, varying from 1 to 2 hr, and is followed by a feeling of well-being. The onset of cardiac pain may be associated with weakness, profuse diaphoresis, hypotension, and a rapid poorly sustained pulse or various arrhythmias A triple rhythm (gallop rhythm) may be present, and the heart tones may be poorly defined.

Inspiratory and expiratory rales and rhonchi may be present over the lung fields. Acute pulmonary edema may be present. The patient may exhibit Cheyne-Stokes respiration as another manifestation of left ventricular failure. Pericardial friction rub may be present, and may occur within a few hours of the attack, but it occurs most frequently during the second to third day. It is heard best medial to the apex or along the left sternal margin. An elevation in temperature occurs within a few hours of the infarction, reaches a peak of 100 to 102°F within 2 to 3 days, and subsides usually within a week. Fever in the range of 104 to 105°F may occur, but this is infre-

ing cove-plane inversion of the T waves; gradual recovery of normal repolarization is marked by progressive decrease in the depth of the inverted T waves and eventual replacement by normal upright T waves. The evolution is usually much slower in infarction than in other types of subepicardial injury.

Preservation of the overlying subepicardial layer in *acute subendocardial infarction* permits registration of the effects of acute subendocardial injury, namely, abnormal sagging or horizontal depression of the S-T junction in overlying leads, with progressive changes in serial tracings Subsidence is manifested by gradual return of the S-T segment to the isoelectric line Residual delay in repolarization of the subendocardial layer may result in broad upright T waves with prolonged Q-T interval.

When there is an antecedent q wave, *notching of the ascending limb of the R* is referable to a defect in conduction in the outer wall of the left ventricle and may be correlated with healed patchy infarction at autopsy

The QRS complex over the area of *subepicardial infarction* commonly shows a reduction in amplitude of the R wave when compared with a tracing taken prior to infarction The Q-T interval is characteristically above the upper limits of normal. there are changes of the S-T junction, S-T segment, and T wave characterized by elevation, descent to isoelectric line, and depression

Subepicardial ischemia or *transmural ischemia* results in transient elevation and straightening of the S-T segment with monophasic upright T, followed by rapid return of the S-T junction to the isoelectric line, accompanied by cove-plane inversion of the T wave The QRS pattern remains normal in serial tracings as long as the ischemic area does not become infarcted, whereas abnormal Q waves appear in the event of extension of the infarct into a previously ischemic area.

Subendocardial ischemia is characterized by a transitory horizontal or downwardly sagging depression of the S-T segment amounting to 0.5 mm or more Reversal in the direction of the T wave is usually secondary to the primary and significant S-T displacement, changes in the direction of the T wave without alteration in the S-T segment are not diagnostic.

The surface relations of the acutely ischemic area may be roughly mapped out from the leads showing the acute S-T depression, e g , localization to leads V_4, V_5, and V_6 indicates ischemia of the *anterolateral wall* of the left ventricle, localization to leads V_7, V_8, and aVF indicates ischemia of the *posterior wall*; localization to leads V_1, V_2, and V_3 points to ischemia of the *septum*.

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In recent infarction with acute subepicardial injury, the S-T junction shows abnormal elevation that changes from day to day, increasing if injury spreads, receding toward the isoelectric line as it subsides; the T wave is at first tall and monophasic, then shows increasing inversion of its terminal portion. With the disappearance of acute injury, the S-T junction becomes stabilized (usually at the isoelectric level), and as organization proceeds, the T wave at first shows increasing cove-plane inversion (*waxing phase*), then a much more gradual decrease in depth (*waning phase*), and finally may return to a normal upright contour. Permanent fixed S-T elevation and cove-plane inversion of the T wave, associated with abnormal QS or QR patterns, occur with healed infarcts that involve a sufficiently large area of the wall to form a *ventricular aneurysm*.

The QRS pattern is of less help in determining age and often remains constant in serial tracings, even though the infarct is recent or organizing. However, significant changes of the QRS pattern, found when adequate technical precautions are taken to ensure against variations in electrode position, constitute evidence of activity. A definite increase in duration and amplitude of the Q at the expense of the R wave at a constant electrode position would indicate *spreading of an underlying subendocardial infarct toward the epicardium*, change from normal QRS complexes at the boundaries of the lesion to abnormal QR deflections would indicate *increase in area of infarction*. On the other hand, abnormal QS and QR patterns found early in the stage of injury may show considerable increase in the R wave at the expense of the Q, *if a portion of the injured myocardium recovers*. Incomplete left BBB is a common finding in recent infarction involving the septum but is often not permanent. Upon its disappearance, a left-to-right septal vector becomes predominant, permitting the registration of Q waves in leads over the left ventricle. The distribution of the infarct in its free wall may then be estimated from the duration and amplitude of these Q waves in comparison with the succeeding R waves.

DIFFERENTIAL DIAGNOSIS

The diagnosis of coronary heart disease may occasionally prove difficult. This may be due to the fact that it *may* coexist with another condition, or the chest discomfort may be *suggestive* but not *typical* of cardiac pain. A large *number* of diseases capable of producing chest discomfort may simulate that caused by coronary artery disease.

These include psychoneurosis, neurocirculatory asthenia, functional disturbances of the gastrointestinal tract, costochondritis or Tietze's syndrome, gastric or duodenal ulcer, chronic cholecystitis and cholelithiasis, esophagospasm, diaphragmatic hiatus hernia, bronchial asthma, *radiculitis secondary* to cervical dorsal spondylitis, displaced cervical disk or posterior spurs associated with osteoarthritis, subacromial bursitis or periarthritis of the left shoulder, cervical rib, scalenus anticus syndrome, metastatic cervical lymph nodes compressing the brachial plexus, pleurisy, pericarditis, aneurysm of the aorta, carcinoma or suppuration of the lung or mediastinal neoplasm, diaphragmatic flutter, and the carotid *sinus syndrome*.

The differentiation of the more benign forms of coronary heart disease from acute myocardial infarction is aided by the increased severity and more prolonged duration of pain, together with the objective laboratory studies which support the latter diagnosis.

The typical history of chest pain precipitated by effort, of relatively brief duration, having a characteristic radiation, relieved when effort is *discontinued* or by nitrites is specifically helpful in arriving at a diagnosis of coronary heart disease in the majority of patients.

Patients with *psychoneurosis and neurocirculatory asthenia usually* present other manifestations of neurosis which are helpful in the differentiation from coronary artery disease. This group of patients may be tremulous, offer *multiple complaints* referable to systems of the *body*, exhibit cool moist *hands and feet and profuse* axillary sweating, and *wear* tinted glasses. Basically the degree of their multiple complaints is markedly out of *proportion* to any objective findings. If *confusion* persists as to the differential diagnosis *in* patients with these manifestations, it will usually be clarified by observing the patient over a significant period of time. Certainly, in this instance, if there is *any* doubt, it is far better to withhold the *diagnosis* of coronary artery disease because *of* the susceptibility of this group of *patients* to suggestion and the danger of converting them *into cardiac cripples.*

Diseases of the gastrointestinal tract such as functional disturbances with gaseous distention, chronic cholecystitis and cholelithiasis, peptic ulcer,

sult in cardiomegaly, pulmonary congestion, pulmonary infarction, pneumonia, or ventricular aneurysm.

Electrocardiogram. The ECG may be normal in patients with the benign type of coronary artery disease, or it may reveal a nonspecific decrease in amplitude of the T waves associated with chronic progressive myocardial fibrosis. In the presence of associated diseases, such as sustained diastolic arterial hypertension, aortic stenosis, or aortic insufficiency, the pattern of *left ventricular hypertrophy* may be present, as well as some degree of *myocardial ischemia,* as reflected by T-wave inversion Acute myocardial infarction usually produces changes in the ECG which make it possible to estimate the distribution of the infarct between the endocardium and epicardium, of its size and location with reference to the cardiac surface, and of its age (Myers).

Electrocardiographic estimation of the distribution of an infarct between the endocardium and epicardium is based chiefly on QRS configuration, but is aided by the S-T pattern in leads from the left precordium, axilla, back, or from the lower esophagus, stomach, or left leg.[15] When the infarct is large, three concentric zones can be distinguished pathologically and usually upon electrocardiographic examination as well: (1) a *central zone* of transmural infarction, extending through the entire wall from the endocardium to the epicardium, (2) a *marginal zone* of infarction confined to a portion of the wall, almost always the subendocardial layer, and (3) an *outlying zone* of ischemia, manifested by pallor and absence of histologic evidence of degeneration If the infarct is small, only the marginal and ischemic zones may be demonstrable

The electrocardiographic findings in leads subtending a central zone of transmural infarction are the following: (1) The registration of an abnormal QS complex in a lead facing the epicardial surface of the left ventricle (which should normally exhibit an R wave as the major deflection) is the characteristic finding when a relatively large central zone of transmural infarction is present in the free wall. (2) Absence of abnormal QS or QR patterns may be encountered despite the presence of transmural or subendocardial infarction.

When the clinical findings suggest infarction, but the ECG yields no confirmatory evidence, the first step is to determine whether or not sufficient leads have been taken to explore the left ventricle adequately. This is especially important when the transitional zone has been displaced into the midaxilla (as a result of right ventricular dilatation and clockwise rotation) for, under these circumstances, *additional back leads* may be needed to cover the left ventricle. Even though the electrode subtends a central zone of transmural infarction, abnormal QS or QR patterns may not be registered for one of the following reasons. a septal vector directed from right to left, as in complete and incomplete left BBB; registration of the ECG soon after the onset of symptoms and before the myocardial changes have progressed to the point of obliteration of the response to the activating impulse (significant S-T displacement without QRS abnormalities is a familiar finding in spontaneous or induced cardiac pain, and repetition of the tracing after a few hours should disclose the development of abnormal QR or QS complexes if infarction is present); patchy infarction with preserved islands of muscle in the subendocardial layer or scattered through the wall.

The findings in leads subtending a marginal zone of subendocardial infarction are the following Characteristic findings are expected when the septal vector is in the normal left-to-right direction and a marginal zone of sufficient size is present Abnormal QR patterns in the left ventricular leads, characterized by an initial downstroke 0.03 sec or longer from onset to nadir and more than 25 per cent of the amplitude of the succeeding R wave, are diagnostic of *transmural infarction.*

Acute injury to subepicardial muscle is manifested by Q-T prolongation and elevation of the S-T segment with a monophasic upright T wave. The upward displacement of the S-T segment is likely to be greater in infarction than in other causes of subepicardial injury and is more likely to be limited rather than diffusely distributed over the right as well as left ventricular leads.

Subsidence of the injury to leave residual abnormalities in repolarization is accompanied by progressive return of the S-T junction toward the isoelectric line, together with increas-

[15] See Chap. 5 *Editor*

he can live comfortably within the limits of [illegible] reserve. Every patient should be [illegible]

[illegible] psychologic factors, mode of living, social and psychologic factors, occupational responsibilities, physical activity pattern, personality traits, and hour-to-hour schedule will provide this specific information. The patient's schedule should be arranged in such a way that he does only what he is capable, leaving a reasonable margin of safety. It is also important to recognize that too strict limitation of privileges beyond that necessary to equalize myocardial supply and demand would not offer complete rehabilitation in the long-term management of the patient with coronary disease Hence the emphasis on individual management in regard to recommendations pertaining to mode of living, rather than a rigid set of rules applied to these patients as a group. It is probably not advisable to restrict the activity of patients beyond the limits which are associated with the precipitation of pain

Since many of these patients have a normal cardiac reserve, they should be permitted to lead a normal life, provided that they do not go in for physical and mental excesses The evidence that mild physical exercise, not sufficient to induce pain, is not harmful and is even beneficial has been suggested by Hefner et al The avoidance of unusually severe activity should be stressed, and this is particularly true in individuals who have followed a sedentary schedule with no regular exercise of any form Many patients with coronary disease who have always carried on an active physical life can still remain quite active after convalescence from a nonincapacitating coronary accident Relatively few patients after a myocardial infarction have to leave their previous occupations The physician should always keep in mind the goal of returning the patient to that type of life which is most economically productive and satisfactory to him and avoid the psychologic hazard of seriously disrupting the patient's life by forcing him to give up work or to change to a less satisfactory occupation The patient's occupation and economic status will admittedly influence this factor, but the psychologic damage may well be as bad as the physical strain, and the goal should be kept in mind

Detailed attention to the proper regulation of the patient's life and habits with the aim of giving him a maximum of satisfaction and happiness *should be the prime objective* of the physician. Since this may involve time-consuming effort, it is often neglected, whereas many doctors tend to overemphasize drug treatment in the attempt to control the symptoms associated with coronary artery disease (Ellis et al.). With detailed attention to the regulation of the patient's life, that is, by cutting out the unnecessary and inefficiently performed details of living, by increasing rest periods during the day or on week-ends, and by taking vacations, his budget of energy can be very markedly conserved Naturally, if he develops symptoms of severe cardiac pain or other complications, his activity will have to be further restricted.

One naturally turns to *vasodilating drugs* in these patients. There is no question that *nitroglycerin* is most effective for the acute relief of individual attacks. There is no agreement as to whether long-acting vasodilators are of specific value in diminishing the number of attacks, and certainly there is no evidence that the routine use of such drugs in patients without symptoms is of any value in diminishing the possibility of future coronary accidents. Therefore, *such drugs should be given only for the relief of symptoms and not as routine measures.* Coronary heart disease is notably affected by psychogenic influences, and many drugs as well as other methods of therapy, if administered enthusiastically and with conviction, will ameliorate the number of attacks in some patients, at least for a time. This undoubtedly explains many of the favorable reports of various methods of therapy and at the same time is a justification for a psychotherapeutic approach to the patients, including the judicious use of relaxant drugs.

Nitroglycerin is the drug of choice since it acts most rapidly. It is administered in tablets which the patient is instructed to dissolve under the tongue The usual therapeutic dose is 1/100 grain, but it is preferable to begin with 1/200 grain. Its action is noticeable in 1 to 2 min and continues for 15 min to an hour In most patients with brief episodes of precordial pain, there is prompt and immediate relief. Sublingual nitroglycerin may precipitate the occurrence of a throbbing headache, and when this occurs, the dose should be reduced. Sublingual nitroglycerin may be used

R wave in the right precordial leads. An alternative rSR' complex may rarely be registered as a variant of the diagnostic QR pattern and has been correlated with extensive infarction of the septum and free wall of the left ventricle.

Left BBB from septal infarction is established from the following criteria: supraventricular origin of the impulse and transmission through the AV node, prolongation of the QRS (0.12 sec or more with complete left BBB; 0.10 to 0.11 sec with incomplete), abnormally late intrinsicoid deflection in *left precordial leads* (0.08 sec or more in complete left BBB; 0.06 to 0.07 sec in incomplete left BBB), initial upstroke in all left precordial leads.

The pattern in right precordial leads indicative of *septal infarction* in the absence of BBB is a qrS complex of less than 0.12 sec, provided due consideration is given to right ventricular hypertrophy and incomplete left BBB. QS deflections of less than 0.12 sec in all right precordial leads also bring up the differential diagnoses between septal infarction without conduction defect and incomplete left BBB. If there is recent septal infarction, the diagnosis may be confirmed by typical S-T evolution in serial records of V_1 and V_2.

INFARCTION OF THE LATERAL WALL OF THE LEFT VENTRICLE. The most common site in the lateral wall is the apical one-third, but most infarcts in this area are extensions of anteroapical lesions, some are continuations of high lateral infarcts, a few represent extensions of posterior infarcts, and a few are primary in the apical portion of the lateral wall. Infarction confined to this area may be manifested by abnormal QR patterns in leads V_5 and V_6 only; infarction extending into this area from other portions of the heart is manifested by abnormal QRS patterns in additional leads, depending upon the distribution of the remainder of the lesion. The most common primary infarct of the lateral wall takes the form of a truncated cone with the base near the AV groove. Large infarcts of this type project sufficiently into the apical third of the lateral wall to produce abnormal QR patterns in leads V_5, V_6, and V_7; smaller infarcts, confined to the basal half of the lateral wall are not detectable in these leads. Signs suggestive of *high lateral infarction* may be present in lead aVL, but the diagnosis is established by abnormal QR complexes (with or without QS patterns) in high axillary leads (HV_5, HV_6, and HV_7).

INFARCTION OF THE POSTERIOR WALL OF THE LEFT VENTRICLE. This is more likely to be missed electrocardiographically than infarction of the anterior or lateral walls because the former is less accessible to exploration by surface leads and more subject to variations in anatomic relations as a result of the changes in level of the diaphragm. The most common primary infarct of the posterior wall takes the form of a truncated cone with the base parallel to the AV groove. If the heart is in a horizontal position, a large posterior infarct may be undetectable in aVF and in leads from the low back and stomach, unless it extends sufficiently into the septum to produce typical signs of septal infarction in these leads. Recognition of infarction of the posterior wall of the left ventricle in such cases must be based upon the patterns in leads HV_7, HV_8, and V_7 and V_8, but a clue as to its presence may be afforded by the reciprocal effects in anterior leads. Smaller infarcts limited to the basal third of the posterior wall of the left ventricle may produce abnormal QR patterns confined to HV_7, HV_8, and V_8 and esophageal leads just below the A-V groove, but not in leads from the stomach or low back (LV_7, LV_5) or left leg (aVF), regardless of the position of the heart.

If the heart is in the intermediate to vertical position, posterobasal or posteroapical infarcts large enough to involve the middle third of the posterior wall should be manifested by abnormal QR patterns in aVF. Complete AV block may accompany massive septal extensions of posterobasal infarction. Secondary *atrial infarction* may be manifested by atrial arrhythmias, but seldom by diagnostic changes in the P or TP waves. Continuation of posterior infarcts into the basal portion of the lateral wall is manifested by abnormal QR patterns in HV_7 and HV_6; continuation into the apical portion of the lateral wall, by diagnostic signs in the customary leads V_7 and V_6. Infarcts involving the apical but not the basal portion of the posterior [illegible] continuations of anterior infarcts [illegible]

[illegible] ally displays evidence of the anterior, and sometimes the septal, portion of the infarct, but not the posterior, unless it involves more than the apical third of the posterior wall. The term *anteroposterior infarction* is applied when the ECG shows evidence of simultaneous rather than consecutive infarction.

Electrocardiographic estimation of the *age of the infarct* is based chiefly on a comparison of the S-T pattern in serial tracings. *Recent infarction* is manifested by progressive changes in the S-T segment and T waves; *healed infarction*, by a fixed pattern in serial tracings. Serial changes in the degree of S-T displacement indicate the presence of injured myocardium that is still living and is destined either to death or recovery. Subsequent serial changes in the T wave have a similar connotation.

blood is more likely to clot 2 to 7 hr following a high-fat intake. The explanation for this is unknown but is not thought to be associated with the lipemia that ensues. Stare advocates that the coronary patient under treatment and the postcoronary individual who has completely recovered get the bulk of his fat and protein calories at breakfast and midday and have a light supper, such as soup, cereal, and a fruit salad.

Regarding evidence that sitosterol or the various lipotropic substances are of value, Stare suggested that, under certain experimental and chemical conditions, they may be limiting factors in fat transport and metabolism, but these conditions have not so far included atherosclerosis or coronary artery disease. Sitosterols, if taken in sufficient quantity and each time food is consumed, will impair the absorption and reabsorption of cholesterol and hence lower the level of serum cholesterol. But the large quantities that must be taken to induce a response, together with the intolerance of many patients to the material (to say nothing of its cost), limit its usefulness appreciably. The administration of sitosterol preparations does not seem of practical importance in decreasing the level of cholesterol.

Long-term use of anticoagulants in patients suffering from coronary artery disease is still in the experimental stage, but it offers a very encouraging avenue of treatment based upon published reports.[18] The mortality rates in the treated groups have varied from 7 to 12 per cent and in the untreated groups from 28 to 33 per cent, an improvement that is quite impressive and certainly a better result than in the short-term treatment of the acute phase [illegible] but it is useful in the treatment of those individuals who clinically manifest a significant degree of cardiac pain or in postmyocardial infarction.

Hypothyroidism can be induced regularly in patients with intractable cardiac pain due to coronary artery disease by radioiodine (Blumgart).[19]

All such patients receive small doses of 6 to 30 mg of thyroid daily to maintain them at the lowest level of metabolism consistent with comfort. Undue elevation of serum cholesterol is reduced thereby and in some patients may be only moderately increased. Approximately three-fourths of all patients treated have shown worthwhile improvement in their symptom of cardiac pain; in one half, the improvement has been great, and many have been restored to an active gainful life. In the other half, the improvement, while not as marked, has been considerable. Patients should be selected who have not responded to the usual medical measures for at least 6 months, whose clinical course is not markedly progressive, and who will be reasonably cooperative. Of all patients who have coronary artery disease, this group comprises less than 5 per cent of the total. From 6 weeks to 6 months is required to produce hypometabolism; consequently this method of therapy should not be invoked in terminal cases. If radioiodine is not available, the *thiourea derivatives* may be used. They do not produce hypothyroidism with regularity, and high dosage may be necessary. Drug reactions are not uncommon.

Hypothyroidism therapeutically induced by I^{131} results in a decrease in frequency and severity of cardiac pain in a significant number of patients with coronary artery disease. On the other hand, the majority of these patients experience symptoms associated with the hypothyroid state: chronic fatigue, intolerance to cold, difficulty in weight control, muscle pain which may be quite severe, [illegible] ing the application of this type of therapy in that group of patients whose occupational responsibilities require higher than average intelligence. In the group of patients so treated and observed by the author, relief of cardiac pain was accomplished in the majority, but most of these patients were not happy and their sense of well-being was not restored because of the associated symptoms of hypothyroidism.

Various considerations lead to the conclusion that the reduction in cardiac work consequent to induced hypometabolism is, in all probability, the most important factor in benefiting these patients. Other possibilities suggested as the mechanisms for the improvement that occurs in intractable cardiac pain after induction of controlled hypothyroidism include (1) a decrease in sensitivity of the cardiovascular system to adrenergic mediators, (2) an alteration in pain perception, and (3) an increased rate of development of intercoronary arterial collateral circulation (Blumgart et al., 1957).

Intensive efforts to develop a technique for

[18] See Part 19, Chap. 8. Editor.
[19] See Part 19, Chap. 8. Editor.

R wave in the right precordial leads. An alternative rSR' complex may rarely be registered as a variant of the diagnostic QR pattern and has been correlated with extensive infarction of the septum and free wall of the left ventricle.

Left BBB from septal infarction is established from the following criteria: supraventricular origin of the impulse and transmission through the AV node, prolongation of the QRS (0.12 sec or more with complete left BBB; 0.10 to 0.11 sec with incomplete), abnormally late intrinsicoid deflection in *left precordial leads* (0.08 sec or more in complete left BBB; 0.06 to 0.07 sec in incomplete left BBB), initial upstroke in all left precordial leads.

The pattern in right precordial leads indicative of *septal infarction* in the absence of BBB is a qrS complex of less than 0.12 sec, provided due consideration is given to right ventricular hypertrophy and incomplete left BBB. QS deflections of less than 0.12 sec in all right precordial leads also bring up the differential diagnoses between septal infarction without conduction defect and incomplete left BBB. If there is recent septal infarction, the diagnosis may be confirmed by typical S-T evolution in serial records of V_1 and V_2.

INFARCTION OF THE LATERAL WALL OF THE LEFT VENTRICLE. The most common site in the lateral wall is the apical one-third, but most infarcts in this area are extensions of anteroapical lesions, some are continuations of high lateral infarcts, a few represent extensions of posterior infarcts, and a few are primary in the apical portion of the lateral wall. Infarction confined to this area may be manifested by abnormal QR patterns in leads V_5 and V_6 only; infarction extending into this area from other portions of the heart is manifested by abnormal QRS patterns in additional leads, depending upon the distribution of the remainder of the lesion. The most common primary infarct of the lateral wall takes the form of a truncated cone with the base near the AV groove. Large infarcts of this type project sufficiently into the apical third of the lateral wall to produce abnormal QR patterns in leads V_5, V_6, and V_7; smaller infarcts, confined to the basal half of the lateral wall are not detectable in these leads. Signs suggestive of *high lateral infarction* may be present in lead aVL, but the diagnosis is established by abnormal QR complexes (with or without QS patterns) in high axillary leads (HV_5, HV_6, and HV_7).

INFARCTION OF THE POSTERIOR WALL OF THE LEFT VENTRICLE. This is more likely to be missed electrocardiographically than infarction of the anterior or lateral walls because the former is less accessible to exploration by surface leads and more subject to variations in anatomic relations as a result of the changes in level of the diaphragm. The most common primary infarct of the posterior wall takes the form of a truncated cone with the base parallel to the AV groove. If the heart is in a horizontal position, a large posterior infarct may be undetectable in aVF and in leads from the low back and stomach, unless it extends sufficiently into the septum to produce typical signs of septal infarction in these leads. Recognition of infarction of the posterior wall of the left ventricle in such cases must be based upon the patterns in leads HV_7, HV_8, and V_7 and V_8, but a clue as to its presence may be afforded by the reciprocal effects in anterior leads. Smaller infarcts limited to the basal third of the posterior wall of the left ventricle may produce abnormal QR patterns confined to HV_7, HV_8, and V_8 and esophageal leads just below the A-V groove, but not in leads from the stomach or low back (LV_7, LV_8) or left leg (aVF), regardless of the position of the heart.

If the heart is in the intermediate to vertical position, posterobasal or posteroapical infarcts large enough to involve the middle third of the posterior wall should be manifested by abnormal QR patterns in aVF. Complete AV block may accompany massive septal extensions of posterobasal infarction. Secondary *atrial infarction* may be manifested by atrial arrhythmias, but seldom by diagnostic changes in the P or TP waves. Continuation of posterior infarcts into the basal portion of the lateral wall is manifested by abnormal QR patterns in HV_7 and HV_6; continuation into the apical portion of the lateral wall, by diagnostic signs in the customary leads V_7 and V_6. Infarcts involving the apical but not the basal portion of the posterior wall are usually continuations of anterior infarcts that involve the apical portion of the anterior wall, the septum, and the posterior wall. The ECG usually displays evidence of the anterior, and sometimes the septal, portion of the infarct, but not the posterior, unless it involves more than the apical third of the posterior wall. The term *anteroposterior infarction* is applied when the ECG shows evidence of simultaneous rather than consecutive infarction.

Electrocardiographic estimation of the *age of the infarct* is based chiefly on a comparison of the S-T pattern in serial tracings. *Recent infarction* is manifested by progressive changes in the S-T segment and T waves; *healed infarction*, by a fixed pattern in serial tracings. Serial changes in the degree of S-T displacement indicate the presence of injured myocardium that is still living and is destined either to death or recovery. Subsequent serial changes in the T wave have a similar connotation.

...lood is more likely to clot 2 to 7 hr following a

...pemia that causes ...

...ary patient under treatment and the postcoronary individual who has completely recovered get the bulk of his fat and protein calories at breakfast and midday and have a light supper, such as soup, cereal, and a fruit salad

Regarding evidence that *sitosterol* or the various lipotropic substances are of value, Stare suggested that, under certain experimental and chemical conditions, they may be *limiting factors* in fat transport and metabolism, but these conditions have not so far included atherosclerosis or coronary artery disease Sitosterols, if taken in sufficient quantity and each time food is consumed, will impair the absorption and reabsorption of cholesterol and hence lower the level of serum cholesterol. But the large quantities that must be taken to induce a response, together with the intolerance of many patients to the material (to say nothing of its cost), limit its usefulness appreciably The administration of sitosterol preparations does not seem of practical importance in decreasing the level of cholesterol

Long-term use of anticoagulants in patients suffering from *coronary artery disease* is still in the experimental stage, but it offers a very encouraging avenue of treatment based upon published reports.[18] The mortality rates in the treated groups have varied from 7 to 12 *per cent* and in the untreated groups from 28 to 33 per cent, an improvement that is quite impressive and certainly *a better* result than in the short-term treatment of the acute phase of myocardial infarction The routine use of anticoagulants in patients with the benign form of coronary artery disease is still not advocated, but it *is useful* in the treatment of those individuals who clinically manifest a significant degree of cardiac pain or *in postmyocardial* infarction

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All such patients receive small doses of 6 to 30 mg of thyroid daily to *maintain them* at the lowest level of metabolism consistent with comfort Undue elevation of serum cholesterol is reduced thereby and in some patients may be only moderately increased Approximately three-fourths of *all patients treated* have shown worthwhile improvement in their symptom of cardiac pain; in one half, the improvement has been great, and many have been restored to an active gainful life. In the other half, the improvement, while not as marked, has been considerable. *Patients should* be selected who have not responded to the usual medical measures for at least 6 months, whose clinical course is not markedly progressive, and who will be reasonably cooperative. Of all patients who have coronary artery *disease, this group* comprises less than 5 per cent of the total. From 6 weeks to 6 months is required to produce hypometabolism, consequently this method of therapy should not be invoked in terminal cases. If radioiodine is not available, the *thiourea derivatives* may ... hypothyroidism

Drug reactions ...

Hypothyroidism therapeutically induced by I^{131} results in a decrease in frequency and severity of cardiac pain in a significant number of patients with coronary artery disease. On the other hand, the majority of these patients experience symptoms associated with the hypothyroid state: chronic fatigue, intolerance to cold, difficulty in weight control, muscle pain which may be quite severe, constipation, hoarseness, pruritus, and coarse, *scaly* skin These patients are "slowed down" mentally and physically This fact is important in considering the application of this type of therapy in that group of patients whose occupational responsibilities require higher than average *intelligence. In* the group of patients so treated and observed by the author, relief of cardiac pain was accomplished in the majority, but most of these patients were not happy and their sense of well-being was not restored because of the associated *symptoms of* hypothyroidism.

Various considerations lead to the conclusion that the *reduction in cardiac work* consequent to induced hypometabolism is, *in all* probability, the most important factor in benefiting these patients Other possibilities suggested as the mechanisms for the improvement that occurs in intractable cardiac pain after induction of *controlled* hypothyroidism include (1) a decrease in sensitivity of the cardiovascular system to adrenergic *mediators*, (2) an alteration in pain perception, and (3) an increased rate of development of intercoronary *arterial* collateral circulation (Blumgart et al, 1957).

Intensive efforts to develop a technique for

[18] See Part 19, Chap 8 *Editor*

[19] See Part 19, Chap 8 *Editor*.

esophageal hiatus hernia, and esophagospasm may usually be differentiated by roentgenologic examination. It should be remembered that gallbladder disease, peptic ulcer, and esophagospasm may coexist with coronary artery disease. The positive history of the relationship of discomfort to effort is helpful in differentiation.

Chest x-ray will be helpful in ruling out scalenus anticus syndrome associated with cervical rib, metastatic cervical lymph node compression, and pulmonary or pleural disease. The *scalenus anticus syndrome* is further recognized by the characteristic circulatory changes which result upon changing the position of the head and extremities.

Pain due to *pleurisy* is characteristically sharp and sticking and bears a definite relation to deep inspiration. Adhesive straping of the chest resulting in limitation of motion of the thorax results in improvement of pleuritic pain. *Bronchial asthma* may be associated with chest pain or a sense of tightness or oppression, but this diagnosis is established by observing the typical respiratory stridor, the prolonged expiration, the typical musical high-pitched rales and rhonchi, the frequent association of bronchiectasis and bronchitis and eosinophilia. *Aneurysm of the aorta* may produce chest pain, but the aneurysm usually presents other manifestations, such as hoarseness and brassy cough, and may be detected by chest x-ray and fluoroscopic examination. In a patient with a syphilitic aneurysm, coexistent involvement of the coronary ostia may be present *Diaphragmatic flutter* may be diagnosed by observing the patient in an attack and by fluoroscopic inspection. The diagnosis of *carotid sinus syndrome* can be established by unilateral massage of the carotid sinus, observing the patient's cardiac rate, blood pressure, and general appearance.

Diseases of the musculoskeletal system frequently present a problem in diagnosis Posterior spurring as a complication of cervical osteoarthritis may result in referred root pain. X-ray of the cervical spine will reveal the presence of this degenerative disease As a therapeutic trial, x-ray therapy to the cervical spine may result in improvement. A *displaced cervical disk* will be documented by x-ray of the cervical spine and oil myelogram. *Subacromial bursitis* or *periarthritis of the left shoulder* is usually associated with restriction of shoulder motion The pain may be maximally localized to the left shoulder bursa, but usually radiates over the deltoid and pectoralis group of muscles, precipitating discomfort in the neck and anterior left upper chest. Examination may reveal a point of maximal tenderness. X-ray of the shoulder may show calcification In the chronic form of this disease, a trial of x-ray therapy may afford improvement. It should be emphasized that subacromial bursitis or periarthritis of the left shoulder frequently coexists with coronary artery disease. Neck traction may be applied as a therapeutic measure in the differential diagnosis of root pain.

The *anterior chest wall syndrome* is a symptom complex of unknown etiology consisting of somatic involvement of the anterior chest wall with pain and tenderness, and often responding well to corticotropin, corticosteroids, or x-ray therapy (Prinzmetal et al.). Palpation of the ribs may disclose a fracture, due perhaps to a metastatic lesion or involvement by a myeloma. Examination of the costochondral junctions, especially on the left side, may demonstrate that the pain is due to arthritis or to a traumatic nonsuppurative painful swelling of one or more of these joints (Tietze's syndrome) (Deane; Benson et al; Wehrmacher).

Brachialgia statica paresthetica, occurring only at night and after the patient has gone to sleep, is also characterized by pain in the arm and transient paresthesia and is attributed to relaxation of the shoulder girdle during sleep and consequent compression of the subclavian artery and brachial plexus between the clavicle and first rib. Deliberate motion of the extremity usually results in disappearance of these symptoms.

Pericarditis may offer a problem in the differentiation of chest pain, particularly since it is accompanied by electrocardiographic changes which may wax and wane and may be of long duration. The age of the patient, the fact that pericarditis may be a complication of another primary disease (tuberculosis, rheumatic fever, bacterial infection), and the clinical course are helpful in documenting this diagnosis.

Predominantly, the typical clinical history suffices to make the differentiation of coronary artery disease from the conditions listed above. The utilization of the exercise or anoxemia test may be helpful. X-ray examination of the lungs and mediastinum, cervical and thoracic spine, ribs, shoulder joints, esophagus, gastrointestinal and biliary tracts may be necessary to reveal the organic basis for pain in the chest, shoulder, arm, or upper abdomen. Certain diseases have been defined which may coexist with coronary artery disease, and these are to be kept in mind.

TREATMENT[16]

Long-term Management of Patients with Coronary Heart Disease. The first principle in the treatment of coronary disease is to adjust the energy budget of the individual so that

[16] See also Part 19, Chap. 3. *Editor.*

istration of these drugs is pain or extreme restlessness.[21] Recurrent or continuing pain is a sign of progressing myocardial damage Occasionally, continuing pain is due to pleural or pericardial irritation rather than to the infarct. Long-continued pain due to the infarction process is often noted in patients who fail to survive Sometimes *Aminophyllin* (0.48 Gm) or *papaverine* (0.03 to 0.09 Gm), given slowly intravenously, will aid in the control [illegible] Sudden death has been associ-

[illegible]

250 ml of 5 per cent glucose in water [illegible] given slowly.

Complete rest, physical and mental, is essential in reducing the cardiac work load. Superior nursing to spare the patient needless *effort* and to encourage equanimity is of utmost importance Bed rest versus chair treatment has now challenged the concept of absolute recumbency and complete *inactivity in the* management of patients with acute myocardial infarction. Prinzmetal pointed out that treatment may become too standardized.

The period of bed rest should be adjusted to the individual case Many patients, even the poor risk ones when not actually in shock, have been described as doing better if allowed to sit in a chair by the bed from the beginning Based upon clinical observations, postinfarction rupture is most likely to occur during the first two weeks and occurs rarely after this period, particularly in mild infarction.

The *diet* for the first day or two of the infarction should be simple, easily digested, and preferably soft or liquid. Unless the patient is hypertensive or in failure, there is no good reason to limit salt drastically His total caloric intake should be relatively low in proportion to his limited activity schedule. It has been suggested that the fat content of the diet be kept low. Kuo and Joyner showed that substernal pain can be easily *induced in some patients* with coronary disease by giving a relatively high fat meal.

As the esophagus passes just behind the heart, very hot or very cold foods should be avoided, or at least taken slowly so the cold or heat, as the case may be, is dissipated. It has been stated that either of these may initiate premature beats and possibly serious arrhythmias. It may be necessary to recommend frequent small feedings rather than three daily meals to avoid satiety and the precipitation of gastrointestinal complaints *Patients should* stop smoking during recovery from acute myocardial infarction Whiskey may be used *in* some cases as a sedative

Constipation is a real problem in most patients with infarction.

Care of bowel function should begin the first day of treatment and not after the patient has gone several days without defecating The use of a detergent (dioctyl sodium sulfosuccinate) in capsules is helpful This substance is not absorbed into the body, can be safely given in effective dosage, and is not a laxative or a purgative. It simply prevents the fecal material from becoming inspissated and hardened Often *one must* use enemas or mild laxation It has been shown experimentally that even in poor-risk patients the use of a bedside commode is safer and less taxing to the circulation than the use of a bedpan.

With the initial medications ordered, *sedation* is useful This may range from simple phenobarbital to the newer tranquilizers. The sedation dosage should be controlled carefully, so that the patient is not overdosed, although mild drowsiness is to be hoped for in the first week at least After this period, the *dose may* often be reduced or eliminated If tranquilizers are used, a check of blood pressure should be made before each additional dose, as many of these preparations may cause a dangerous drop in blood pressure. For sedation at night, if needed, *chloral hydarte* seems to work well and can be used in those patients who are found to do poorly on the barbiturate derivatives *Bromides* are often useful where barbiturates are poorly tolerated

The use of *nitroglycerin* in acute myocardial infarction has not been *scientifically* defined

[21] Morphine also produces the effect of depressing the central nervous system and decreasing the metabolism The first is a useful result because it decreases *the possibility* of dangerous reflexes The second is also useful because it decreases *cardiac work* Thus, the use of morphine or some other form of sedation is recommended by many, even in the absence of pain, for the first 5 to 15 days from the beginning of the *attack Gradual* substitution of morphine or Demerol with barbiturates is recommended, both in order to prevent habituation and in order to avoid too sudden discontinuance of effect. *Editor*

prophylactically to avoid the occurrence of cardiac pain in those patients where the precipitation factor is constant. Nitroglycerin is also available in a sustained-action tablet *Nitroglyn* for oral use, containing 1/25 or 1/10 grain and designed to be released uniformly for a period of 10 to 12 hr. A tablet at breakfast and bedtime is said to prevent or greatly diminish attacks of cardiac pain. *Amyl nitrite* acts more rapidly, within 10 to 15 sec, but its action lasts only for several minutes. It is administered in small glass pearls or ampuls which must be broken and inhaled. The use of *nitroglycerin ointment* locally has been described as affording relief. During a period beginning about 30 to 60 min after application of the ointment and extending up to 2 to 4 hr, the amount of effort required to induce chest pain has usually been definitely increased (Hefner et al.).

The long-acting nitrates have occasionally seemed to have a striking effect, but much more often the results have been disappointing. These include *erythrol tetranitrate*, which may be given orally as tablets in doses of 0.015 to 0.030 Gm (1/4 to 1/2 grain) and requires 15 min for effect, the duration of which is several hours. *Mannitol hexanitrate* and *mannitol pentanitrate*, the action of which is even more delayed and prolonged, may be given in 1/4- to 1/2-grain doses for prophylactic effect *Peritrate (pentaerythritol tetranitrate)* is a long-acting nitrate, available in 10-mg tablets, and is administered in doses of one or two tablets three or four times daily. The prophylactic action is said to begin 1 1/2 hr after a dose and to last 4 to 5 hr *Triethanolamine trinitrate (Metamine)* administered in doses of 2 mg four times daily is another long-acting nitrate.

The most commonly used xanthine preparations are *theophylline with ethylenediamine (Aminophyllin)*, 0 1 to 0 2 Gm, *theobromine sodium salicylate (Diuretin)*, in doses of 0 3 Gm; *theobromine calcium salicylate*, 0 5 Gm; and *theobromine sodium acetate*, 0 5 Gm three to four times daily. All these preparations may induce nausea in some patients and in others may not lead to any discernible improvement. In patients with attacks of nocturnal cardiac pain, diuretics have been advocated as being useful. *Quinidine sulfate*, 0.3 Gm four times daily, has been reported as being of value. Its duration of action is approximately 6 hr *Sedatives*, such as *phenobarbital* in doses of 0 015 to 0.03 Gm (1/4 to 1/2 grain) three times daily, are frequently employed.

The so-called *ataractic* or *tranquilizing drugs* have been administered instead of the established sedatives. Their benefit is to reduce anxiety tension.

Papaverine has been recommended in oral doses of 0.1 Gm four times daily on the basis of its vasodilator effect and its sedative action. *Dioxyline phosphate (Paveril Phosphate)* is a synthetic preparation related to papaverine. The recommended dose is 0.2 to 0.4 Gm three to four times daily.

Practical *dietary management* of patients with chronic coronary disease is indicated in the therapeutic management.[17] Nutritional research suggests a number of specific dietary approaches that may be helpful in the management of patients with coronary artery disease (Ellis et al.). First, attention should be given to *weight reduction*, particularly if the patient is overweight. But, even if he is of desirable weight, a loss of as little as 3 to 5 lb is frequently accompanied by a decrease in serum cholesterol of the order of 10 to 15 per cent.

This decrease may not be maintained when caloric equilibrium is reestablished but, if not, other dietary therapy may be tried. No single food need be eliminated from the diet. It simply is a matter of eating less: cutting down, not out (smaller portions, no seconds, common sense), and checking by a weekly stand on the bathroom scale. Second, in addition to advising weight loss, the physician might propose that the patient try a diet in which the total calories derived from fat are reduced to 25 to 30 per cent. Such a diet would entail a reduction of most of the visible saturated fats. This can be accomplished by trimming fat from meat, eating more lean meats and smaller servings, more fish, and consuming less butter, margarine, whole milk, cheese (except cottage), bacon, and egg yolks. Another dietary regimen that can be tried is one that provides the accustomed 40 to 45 per cent of calories from fat but in which the fats that are good sources of essential fatty acids are emphasized, so that they might supply about 25 per cent of the fat calories or 10 per cent of the total calories. Ellis et al. state that it has been difficult to increase further the essential fatty acids without using formula diets.

If the patient is acutely sick from one of the complications of atherosclerosis, therapy might include a *very low fat diet* (one with 20 per cent or less of the calories coming from fat). Also, for the sick patient a formula-type diet might be tried containing a suitable *vegetable oil* as the sole source of fat. The avoidance of excessive fat, particularly in the evening meal, may be desirable from the viewpoint of decreasing the chances of intravascular clotting It has been established that

[17] See Part 19, Chaps. 4 and 5. *Editor.*

approximately two to three times the normal standard for the Lee-White method Blood should be drawn 2½ hr following the initial injection. If the clotting time is less than 15 min, 75 mg of heparin is given at the next dose When the clotting time has been stabilized within the therapeutic range, the dosage is adjusted to maintain the stability. Blood for prothrombin time is taken just before the next dose of heparin is given

Continuous Intravenous Drip. For this method, 100 or 200 mg of heparin sodium is added to 1,000 ml of a sterile solution of either 0 9 per cent saline or 5 per cent dextrose and given by intravenous infusion by means of a 20-gage needle Initially, the flow of the solution is adjusted to run at a rate of 60 drops per minute and later slowed to a sufficient rate to maintain the blood-clotting time between 20 and 40 min These estimations should be done not less than every 2 hr until the desired range is well established, after which it need be done less frequently Prothrombin time estimation is of no value when heparin is given by this method and should, therefore, be postponed for at least 4 hr after the infusion has been discontinued Continuous intravenous fluid administration may be contraindicated in patients with severe pulmonary edema and/or cardiac decompensation.

Subcutaneous and Intramuscular Injection Concentrated aqueous solution of heparin, 200 mg/ml, is given by deep subcutaneous injection into either the thigh or the buttocks The repository type of solution (*Depo-heparin*) takes advantage of the action of gelatin and dextrose in retarding the absorption of heparin Its anticoagulant effect is produced within 2 to 4 hr, and blood-clotting time estimations are made 4, 8, and 12 hr following injection If the clotting time is less than 20 min, another injection of 200 mg is given At times a larger initial dose of 400 mg may be indicated By this route, it is possible to reduce the number of injections to two, and sometimes only one, in a 24-hr period An effective therapeutic blood-coagulation time of three times the normal value should be maintained Intramuscular heparin, to which 100 turbidity reducing units of hyaluronidase has been added, has very little effect in prolonging blood-clotting time (Tronnberg)

At the time the initial dose of heparin is administered, the initial dose of *Dicumarol* (or one of its congeneric substitutes) is also given by the oral, subcutaneous, or intravenous route, depending on the drug used Ordinarily 18 to 72 hr is required to produce a desired prothrombin time of 2 to 2 5 times normal With anticoagulants having a rapid induction time, only three or four doses of heparin may be required before the prothrombin level is reached; then the heparin can be discontinued.

Maintenance of an effective prothrombin time can be accomplished in two ways: (1) a daily dose given at one time or in divided doses over the 24-hr period, (2) intermittent dosage, whereby medication is given only when the prothrombin time drops to its lowest effective therapeutic level, the cycle being repeated as indicated. This wide swing in prothrombin time makes the interrupted method less effective than the daily-dose method. Once a prothrombin time of 2 to 2 5 times normal is attained, the amount of drug necessary to maintain it will depend upon the particular anticoagulant being used and the patient's response to it.

It is axiomatic that anticoagulants are withheld in the presence of a rising prothrombin time Beyond the upper limit of therapeutic effectiveness of the prothrombin time, the number of bleeding episodes is nearly doubled in frequency without statistical evidence of improvement in the incidence of thromboembolic complications *When the control time is 12 to 13 sec, the induced prothrombin time in the patient should range between 25 and 40 sec* With the establishment of a proper maintenance dose, prothrombin times need no longer be done daily Possibly every 3 to 4 days will suffice, unless otherwise indicated. If proper control is available and there are no contraindications, the patients should be kept on anticoagulants for a minimum of 30 days

Contraindications to the use of heparin and other anticoagulants are (1) preexisting tendency to bleed (hemophilia, purpura, etc.), (2) bacterial endocarditis, (3) ulcerative lesions, especially in the gastrointestinal tract, (4) suspected intracranial hemorrhage,[23] (5) threatened abortion, and (6) hypersensitivity to the drug Additional contraindications to certain anticoagulants are (1) recent operations on the brain or spinal cord, (2) regional anesthesia and lumbar block, (3) severe hepatic disease and known vitamin K deficiency with bleeding Great caution should be exercised in dealing with patients with severe hyper-

[23] Subsequent favorable experience with anticoagulants in cerebrovascular accident and the reasonable doubt raised in regard to the actual frequency of "cerebral hemorrhage" have decreased the value of this contraindication *Editor.*

the *revascularization of the ischemic heart* have been in progress.[20] The surgical therapy of coronary artery disease is designed to accomplish two things: (1) the amelioration of the symptoms of cardiac pain and (2) protection against ventricular fibrillation, in the event of a future coronary occlusion, by the introduction of relatively small quantities of blood to the ischemic myocardium through extracoronary collateral circulation. Many surgical methods have been worked out in the animal laboratory that protect against coronary occlusion. Such procedures have relieved cardiac pain in some patients. The question is which one is most likely to bring a new blood supply to the heart of the patient with coronary disease and which can be performed with the greatest safety to the patient.

Treatment of Acute Myocardial Infarction. In view of the excellent prognosis in the mild cases, it seems neither necessary or desirable to restrict the activities of these patients to the extent warranted in the more serious cases For the first 2 weeks after onset, the patient is treated in the usual manner, either in bed or in a chair. At the end of this period, a gradual resumption of normal activities is begun Every attempt is made to avoid stressful situations, emotional as well as physical. If no untoward incidents occur, the patient is allowed to return to work under the close supervision of the attending physician. If the situation progresses satisfactorily, the patient is allowed to increase his work by 1 hr per day during the second week He is then reexamined at weekly intervals for the next month If, at any time, unfavorable signs or symptoms appear, the patient is returned to bed and the entire situation is reevaluated. If the classification is questionable in any given case, the patient is treated in the conventional manner It also may be inadvisable to depart from the usual method of treatment if the patient or his family is apprehensive about early resumption of activity

In contrast, patients who have severe or repeated bouts of pain, marked drops in blood pressure, marked leucocytosis, high elevations of the erythrocyte sedimentation rate and of serum transaminase levels, high and prolonged temperatures, congestive failure or arrhythmias requiring treatment are classified as "severe cases."

The "poor-risk" patient, by definition, is one who has, besides an infarction, one or more of the following complications of this disease persistent and intractable pain, shock, congestive failure, and serious arrhythmias, such as atrial flutter or fibrillation, nodal rhythm, ventricular tachycardia, and conduction defects. All these need prompt and definite therapy if the patient is to survive. The most valuable aid in the treatment of myocardial infarction is prompt diagnosis Where infarction is suspected, it is well to treat the case as such until proved otherwise.

The medical aims of treatment in acute myocardial infarction may be listed as follows:

1. The relief of pain
2. Prolongation of life until healing occurs by:
   - *a.* Reduction of cardiac work load
   - *b.* Prevention of spread of infarction
   - *c* Treatment of shock, failure, or both
   - *d.* Prevention or treatment of serious arrhythmias
   - *e* Prevention of thromboembolism

Reassurance and cheer must be a part of the therapy to combat apprehension, fear, or intense worry. The problem of visitors is a serious one It is poor policy to allow more than the immediate family to see the patient for at least the first 2 to 3 weeks Aside from the psychogenic aspect, the effort in talking with and entertaining visitors is a strain on the patient. Even members of the immediate family should be limited in visiting time

Pain should be treated promptly either by parenteral use of *morphine* (or one of its derivatives) or *Demerol* (meperidine). Meperidine relieves pain but does little to relieve the individual's fear or apprehension. For this reason, morphine is preferred in most cases. However, it may cause nausea and vomiting, and sensitive patients usually do not tolerate any opium derivatives. If morphine is tolerated well, one may give *atropine* or *scopolamine* with it to block the vasovagal effects of the pain Meperidine works well in most elderly patients and seems to have a wide safety factor A new drug *Paracodin* seems to be midway between morphine and Demerol when used parenterally. The indication for admin-

[20] See Chaps. 9 and 10 *Editor*

produced recovery by the time pain has been relieved, vasopressor drugs are administered. *Levarterenol* (*Levophed*) appears to be the most potent pressor agent Eight milligrams is added to the glucose infusion, and the drip is regulated at a rate sufficient to elevate the systolic pressure to about *100 mm Hg pressure*. After the desired pressor effect *is obtained*, the drip is maintained at about 1 ml/min or less

[illegible]

sion if more is required to maintain the [illegible] rather than to increase the rate of drops per minute. When protracted therapy becomes necessary, it is wise to insert a polyethylene catheter into an arm vein to avoid leakage and a consequent slough in the tissues As soon as possible after the Levophed is started, a urinary catheter is inserted, the bladder is emptied, and the rate of urine flow is determined Agress has found this a sensitive indicator of the degree of shock and the progress of the patient. In general, the rise in systolic pressure, the widening of the pulse pressure to 20 mm Hg or more, and the increase in urinary flow indicate a favorable response to the dosage used

Methoxamine (*Vasoxyl*) metaraminal (*Aramine*), phenylephrine (*Neosynephrin*), mephentermine (*Wyamine*), and *ephedrine* are other vasopressor agents in current use Levophed administration is limited to the intravenous route, and sloughing of the skin is an occasional complication in continued therapy Aramine is a new vasopressor which can be administered intramuscularly as well as intravenously and is useful for prolonged administration because leakage into the tissues does not produce a slough

Reported experience with *intravenous* and *intraarterial transfusions* indicates that neither of these measures lowers the mortality rate of severe shock associated with acute myocardial infarction Preliminary experience with *thoracic epidural analgesia* suggests that this measure may be of value in otherwise intractable shock (Agress)

ARRHYTHMIAS Disturbances of rhythm are common in patients with acute myocardial infarction It has been found that approximately one-half of these patients develop disturbances in the blood supply to the heart which may have effects on the cardiac rhythm (Scherf). *Extrasystoles occur most* commonly in myocardial infarction. These may subside with the administration of oxygen and drugs which relieve pain and anxiety. If they persist in significant degree, *quinidine* in a dosage of 0.2 Gm every 4 to 6 hr may be prescribed. If the extrasystoles are not controlled, the time interval may be shortened to every 2 hr and then a maintenance schedule of every 4 hr followed.

Quinidine has been recommended in the routine prevention of extrasystoles in acute myocardial infarction, but the effectiveness of prophylactic treatment is highly controversial and has not been universally accepted in the general-treatment regimen.

The occurrence of *paroxysmal tachycardia* may result in fall of blood pressure, increase of venous pressure, hepatic and pulmonary congestion, myocardial ischemia, and collapse. *Atrial paroxysmal tachycardia* is uncommon. It is generally associated with evidence of atrial infarction (elevation of the P-R segment). In about one-half of the cases, the arrhythmia can be stopped by carotid pressure or one of the other vagal reflexes. If none of these is effective, *quinidine* is worthy of trial. A rapidly acting digitalis preparation such as *Cedilanid* (0 4 mg) or *strophanthin* (0.25 mg of ouabaine or Strophosid) has also been reported as being effective Whereas intravenous strophanthin acts within minutes, Cedilanid or digoxin is effective within a half hour. It is well to apply again the various vagal *reflexes at the height* of the digitalis effect since, at that time, they are often successful. *Ventricular paroxysmal tachycardia* carries a grave prognosis since it leads to a mortality of about 50 per cent. Quinidine may be tried, but in many cases has been without success Procaine amide (*Pronestyl*) may be administered intramuscularly or intravenously, and its use has been followed by good results The rate of the intravenous injection should not exceed 50 mg/min, and the total dose should be *no greater than* 1 Gm. The administration must be stopped if the blood pressure falls during the injection.

During the *injection*, the rhythm should be monitored by the ECG Some patients fail to respond to either quinidine or procaine amide. In such cases, the treatment should be the same as in *atrial* tachycardia, utilizing digitalis or strophanthin. *Atrial flutter* is rare but *fibrillation* is seen in about 8 per cent of pa-

as to its benefit or danger. The hazard of blood pressure reduction makes its use potentially dangerous.

If used, it should be given cautiously. An initial dose of 1/400 grain every 2 hr with observation of the blood pressure has been suggested by Hefner et al. If a significant decline in blood pressure occurs, which is rare as long as the patient remains recumbent, dosage is decreased, otherwise, dosage is increased to about 1/200 grain every hour. No unfavorable changes in the patients treated by this method have been observed. Longer-acting nitrate preparations have been utilized, but their beneficial effect has not been defined. Russek and coworkers advocated *Peritrate* as the choice of a coronary vasodilator.

In the presence of shock, heart failure, or cyanosis, *oxygen* is a most important agent, and at times it seems useful for the patient with long-continued pain. It is indicated in all moderate or severe cases and always when the pain is resistant to other measures. Dyspnea is relieved, pain is lessened, the heart rate is slowed, and not infrequently the patient soon lapses into quiet, restful sleep.

Digitalis should be administered to all patients with evidences of congestive failure or with rapid ventricular rate due to atrial fibrillation or atrial flutter In the absence of definite indications, it is unwise to use digitalis. The rapid absorption of some of the purified glycosides, such as *digitoxin* or *digoxin*, frequently obviates the necessity of parenteral administration.

Rapid digitalization can be accomplished by 0.6 mg of digitoxin followed by 0.2 mg after 2 hr and then by 0.2 mg every 4 hr until the desired effect is attained The average total digitalizing dose is about 1 2 mg, and the average daily maintenance dose is 0 15 mg

Quinidine sulfate has been advised routinely to minimize the possible development of paroxysmal tachycardia or fibrillation. The drug is not without occasional adverse effects, causing nausea, vomiting, or diarrhea in some patients; in moderate dosage, it may also cause a drop of blood pressure in some patients with acute myocardial infarction. In the presence of extrasystoles, however, its administration should be attempted in doses of 0 2 Gm every 3 or 4 hr. If gastrointestinal symptoms are induced, enteric-coated preparations or the administration of the drug parenterally is indicated.

There is complete agreement that *anticoagulants* have a definite place in the management of acute coronary thrombosis with myocardial infarction. There is no disagreement as to the principle and value of the treatment but only as to its application in particular cases

Medication should be started at the earliest possible moment in mild or good-risk cases rather than being withheld until complications develop, always presupposing that there are not contraindications to their use and that proper control is available. Certain groups favor anticoagulants in the "poor-risk" group but raise serious doubts concerning the ability to determine accurately the prognosis in the earliest stages of acute coronary thrombosis.

The over-all mortality rates in controlled studies of anticoagulant therapy in acute myocardial infarction strongly suggest that *anticoagulants should be employed routinely in this disease*. Omission of anticoagulants is justified today only by lack of laboratory facilities to perform accurate prothrombin determination or the presence of definite contraindications. The reason for this recommendation is because mild cases or good-risk cases cannot always be accurately distinguished at the very onset of the illness. If anticoagulant therapy is beneficial in the treatment of seriously ill patients, this benefit should also be afforded to those who appear less seriously ill

Skillful employment of the anticoagulant treatment of acute myocardial infarction demands an adequate knowledge of the physiology of the blood-clotting mechanisms,[22] complete familiarity with the anticoagulant or anticoagulants being used, and dependable laboratory facilities.

During the first phase of treatment, *heparin* will be the preferred drug and can be administered by one of the following three methods

Intermittent Dosage. By this method, 50 to 75 mg of heparin sodium dissolved in 25 to 50 ml of 0 9 per cent sterile sodium chloride, 5 per cent dextrose, or distilled water is given by slow intravenous injection and repeated at intervals of 3 to 4 hr, depending upon the blood-clotting time. The dosage should be adjusted to maintain the blood-clotting time between 15 and 20 min, which is

[22] See Part 2, Chap. 28 *Editor*.

In the treatment of arrhythmias due to digitalis, Lown and Levine suggest a *schedule as follows:* a dose of 5.0 Gm of potassium chloride is given by mouth. If within an hour there is no reversion, Pronestyl is given intravenously, 50 mg every 1 to 2 min, with blood pressure determinations and electrocardiographic monitoring during the injection. Pronestyl may be administered orally. After an initial dose of 1.0 Gm, 0.5 Gm is given every 3 to 6 hr.

The duration of *convalescence* and the decision as to whether and when a gainful occupation may be resumed must be determined individually in each case. Patients with pronounced and persistent symptoms of congestive heart failure, with cardiac pain recurring frequently at rest, after minimal effort, or with extreme weakness, may require an indefinitely prolonged period of convalescence. Psychotherapy *often becomes a dominant element in* medical management. The physician should not enforce prolonged invalidism merely because the patient has experienced a severe attack. Patients who recover from the acute attack, and who experience little or no distress as they become ambulant, should nevertheless spend a variable period after recovery in gradually resuming normal care of themselves in the home and in taking short walks outdoors. The *resumption of* physical exertion after convalescence must be determined by careful evaluation. Persistence of symptoms may be due to extensive myocardial infarction and congestive heart failure or may often be the consequence of inactivity and poor muscular tone. A fair trial should be made under close observation to determine whether the response to a graduated regimen is favorable or not. Many patients will be well enough to return to their previous work and engage in all their normal activities, although "moderation" should be recommended.

Economic as well as medical considerations often dictate the extent to which the patient can modify his type of work, the conditions and hours of his employment, and the periods of rest. In many cities, there are *cardiac work classification units,* in which a coordinated effort by a team of cardiologist, psychiatrist, social worker, and other professional workers serves to determine the patient's capacity for work, to help in his gradual rehabilitation, and to aid him in finding suitable employment.[28]

[28] See Part 20, Chap. 2. *Editor*

tension, active pulmonary tuberculosis, renal failure, debilitating disease, and cachexia.

The clinician must be acquainted with the complications of anticoagulant therapy. *Hemorrhage* is the most common, occurring in 9.2 per cent of the cases (Wright et al.). *Toxicity* is usually due to improper use of the drugs, although bleeding does occur in the presence of a prothrombin time which is not too retarded. Gross or microscopic *hematuria* is the most frequent of the bleeding manifestations of toxicity. Usually it clears without permanent genitourinary tract damage when the drug is withdrawn or other measures are applied. *Hemoptysis* occurs occasionally; and, when it is present, pulmonary embolism and congestive failure must be considered in the differential diagnosis. Bleeding from the gastrointestinal tract (either as *hematemesis* or *melena*) is seen most often in patients with ulcerative lesions, neoplasms, or hemorrhoids. *Epistaxis* occurs in about 1.5 per cent of the cases. *Hemopericardium* should be suspected when there is evidence of one or all of the following findings: (1) recurrence of chest pain without electrocardiographic evidence of extension of a recent myocardial infarction; (2) persistent pericardial friction rub; (3) circulatory collapse accompanied by drop in blood pressure, sudden hepatomegaly, and distended neck veins; (4) sudden unexplained anemia, and (5) x-ray evidence of pericardial effusion (Izzo et al.)

Published data indicate that *myocardial rupture* occurs more frequently in the anticoagulant-treated than in the untreated cases. Lee and O'Neal state that myocardial rupture occurs five times more frequently in anticoagulant-treated cases. Cerebral hemorrhage can be a serious complication in the presence of bacterial endocarditis, and anticoagulants should be used with caution. *Paraplegia* has been reported following excessive use of Dicumarol, probably on the basis of hemorrhage into the central nervous system (Arieff et al.). Chatterjea and Salomon report an antagonistic effect of ACTH and cortisone on the anticoagulant effect of Tromexan. To maintain effective prothrombin levels, patients receiving these steroids often required larger doses of Tromexan, when steroids were discontinued, smaller doses of this anticoagulant were needed

Long-term anticoagulant therapy is an extension of the first and second phases of the treatment of acute myocardial infarction and requires the same meticulous care and vigilance. Indications (Shapiro) for its use are (1) continuing precordial pain after recovery from myocardial infarction; (2) recurrent myocardial infarction, especially if thromboembolic complications are evident; (3) development of recurrent and severe cardiac pain suggesting an impending coronary occlusion, following an asymptomatic postinfarction period (Keys et al., 1953); (4) cardiac arrhythmias with embolism; and (5) chronic congestive heart failure.

The *prophylactic use of antibiotics* has been advocated in the immediate treatment of acute myocardial infarction. There are no well-controlled statistical studies to indicate whether or not the administration of *penicillin* prophylactically results in a decreased incidence of pneumonia. Until further proof, it is recommended that antibiotics be withheld until specific indications for their use become manifest in the patient.

Treatment of Complications. SHOCK. Shock is one of the serious complications of myocardial infarction and occurs in about 12 per cent of the cases (Binder et al.). Mild and moderate forms of shock have a low mortality and often require no treatment but the relief of pain and the administration of oxygen. Modern treatment has reduced the mortality for severe shock from 80 to 60 per cent, largely by the use of vasopressor drugs (Agress). In the management of the patient, the first aim should be to relieve pain by the administration of narcotics. With the decrease in mean arterial perfusion pressure, absorption from the tissues is greatly diminished, so that much more relief from pain is obtained by administering the narcotic intravenously. At the same time, oxygen is administered through a nasal catheter or BLB mask at the rate of 6 to 8 liters. If the lungs are not congested and orthopnea is absent, the foot of the bed is elevated. If pulmonary edema is present, the head of the bed is raised to the position of optimal comfort.[24] Positive pressure breathing is avoided unless pulmonary edema is severe, because of its frequent effect of lowering blood pressure. If these measures have not

[24] See Part 18, Chap. 14. *Editor.*

tivity and the erythrocyte sedimentation rate, the white blood count, or the C-reactive protein levels. The type of hemolysis occurring during routine separation of serum from red blood cells does not significantly alter SGO-T and SGP-T activity but causes a significant increase in *SLD*

Since SGO-T activity has been studied in many more patients with heart disease than SGP-T or SLD, only brief mention of changes in the activity of the latter two enzymes will be made where data are available for comparison

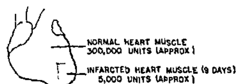
MYOCARDIAL INFARCTION

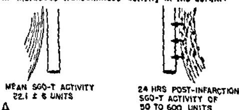
Experimental. Myocardial infarction was produced in dogs by the injection of plastic spheres into the coronary sinus In every experiment, the SGO-T activity rose promptly, with peak levels appearing 9 to 23 hr postinfarction, sometimes reaching values 20 to 30 times control levels There was a relatively linear correlation between the amount of infarction estimated at autopsy and the maximal rise in SGO-T activity (peak level) The animals with the highest SGO-T levels had the greatest degree of myocardial infarction Acute myocardial necrosis produced by the intravenous injection of papain in rabbits resulted in peak SGO-T levels in individual experiments that were again roughly proportional to the degree of necrosis found at autopsy.

Myocardial infarction was also produced in dogs by tightening a ligature 10 days after it had been placed about a coronary artery Fifteen infarcts produced by this method were all associated with an increase in the SGO-T activity As in the previous experiments, the higher the SGO-T activity, the larger the infarct, for example, the SGO-T peak from a 0 5-Gm infarct was 64 units (24 above normal) and for an 18-Gm infarct, 500 units

The duration of abnormally increased but falling SGO-T activity was 4 to 5 days in animals with large infarcts and 24 hr when smaller areas of infarction were produced Thus, both the height and duration of increased enzyme activity appeared to be proportional to the size of the infarct Analysis of the homogenates of the infarcted heart muscle showed a progressive decrease in GO-T activity with time which was proportional to the age of the infarct Uninfarcted muscle from the same animal showed normal concentration of GO-T

In similar experiments on seven dogs given 5- to 60-Gm infarctions, the SGO-T activity increased 3 to 10 times, the SGP-T 3 to 5 times, and the SLD 2 to 3 times normal.





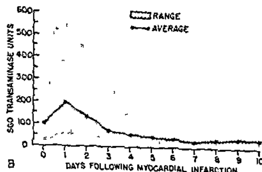


Fig 10-5. A. The probable mechanism of increased serum glutamic oxaloacetic transaminase activity following acute myocardial infarction B The range (stippled area) and average (solid line) serum glutamic oxaloacetic transaminase activity following the onset of acute transmural myocardial infarction in 300 patients

Clinical. Serums secured within 12 to 48 hr after the onset of unequivocal *acute transmural myocardial infarction* and daily thereafter in 300 patients have been analyzed for GO-T activity In all but three instances, when the serum was obtained at the time of acute infarction, the SGO-T activity rose 2 to 20 times normal within the first 48 hr (Fig. 10-5B) The height and duration of increased SGO-T activity appeared to be roughly proportional to the size of the infarct as estimated electrocardiographically. Secondary elevations of SGO-T were seen following recurrent chest pain due to extension or the development of a new infarction in the same patient

In 50 patients with acute transmural myocardial infarction who had studies of the activity of all three enzymes, the SGO-T rose 2 to 20 times normal, the SLD 2 to 10 times normal, and the SGP-T 1 to 3 times normal.

tients with acute myocardial infarction. When the ventricular response is slow, there is no disturbance of circulation and the arrhythmia usually disappears in a few days with (and often even without) quinidine therapy. If, on the other hand, the ventricular rate is rapid, an emergency is present and immediate treatment is indicated. The response is generally rapid.

The method of choice is the intravenous administration of *Digilanid* (0.4 to 0.8 mg), digoxin (1.0 to 1.5 mg), digitoxin (0.5 mg), or strophanthin (0.25 mg). Even if flutter or fibrillation does not disappear after administration of the first dose, the ventricular rate may be slowed Daily repetition of the above doses will in most cases restore sinus rhythm within a few days *Ventricular flutter* can hardly be differentiated from paroxysmal ventricular tachycardia Of all the arrhythmias, *ventricular fibrillation* is the most dangerous. It has been possible, in some instances, to effect defibrillation either by electric shocks or by massage of the exposed heart, in combination with the use of Pronestyl

Sinus *bradycardia* may be present due to an increased vagal tone. Atropine sulfate intravenously in doses of 1 mg has been recommended The very slow ventricular rate, however, may be due to complete AV dissociation. Vasopressor therapy may then increase the arterial perfusion pressure so that coronary flow improves sufficiently to decrease myocardial ischemia and allow normal conduction *Isuprel* can be given in intermittent intravenous doses of 0.02 to 0.04 mg or in a continuous intravenous drip containing 1 2 to 2 0 mg in 500 ml of 5 per cent glucose solution Used under these circumstances, Isuprel has been found to potentiate the pressor effect of Levophed (Agress) In its simplest form, AV block may merely be a prolongation of the P-R interval and may not cause a disturbance of rhythm In AV block and BBB, administration of quinidine is contraindicated Attacks of ventricular fibrillation have often been observed under this medication; sudden death is common.

The most dangerous phenomenon developing in heart block caused by myocardial infarction is the *Morgagni-Stokes-Adams syndrome*.[25] Frequently, when partial block changes into a complete block, the automaticity of the deeper centers of the myocardium does not develop in time to prevent unconsciousness. This may occur once or several times or even last for days. There are other mechanisms responsible for this syndrome. Ventricular tachycardia and paroxysmal ventricular fibrillation can also cause unconsciousness with convulsions, and not infrequently the ECG taken during an attack will show a combination of arrhythmias Bellet and his coworkers recommend the intravenous injection of molar sodium lactate. The dose employed ranged from 15 ml of molar sodium lactate administered intravenously in 1 min to 960 ml molar and half-molar solution in 5 hr, according to the urgency of the situation and the response. The use of external electrical stimuli has been recommended by Zoll and his group.[26]

Treatment of *acute left heart failure* in myocardial infarction consists primarily of rest, oxygen with antifoaming therapy,[27] morphine, tourniquets, and digitalis. *Antifoaming (or defoaming) therapy* using ethyl or capryl alcohol in the humidifier bottle is advocated. The oxygen flow should be 2 to 3 liters/min at first and then 10 liters/min, with alternate periods of inhalation for 30 or 40 min (Luisada et al.; Pollock).

Treatment of *chronic congestive failure* in myocardial infarction consists primarily of rest, low sodium intake, digitalis, oxygen, and diuretics. The usual indications for the use of digitalis are well recognized: (1) congestive heart failure, either left, right, or a combination, resulting from defective myocardial contraction, excessive ventricular rate, or both, (2) forward failure where cation retention is primary; and (3) the treatment or prevention of various cardiac arrhythmias or disorders of cardiac mechanism characterized by a rapid ventricular rate, such as atrial flutter or fibrillation Ventricular extrasystoles or ventricular tachycardia have been observed to subside following digitalization in the presence of acute congestive failure. It is generally unwise and unnecessary to treat acute or chronic congestive failure in myocardial infarction by parenteral routes unless (1) acute pulmonary edema is present or (2) there is no other feasible portal of entry (Bine).

[25] See Part 11, Chap. 6. *Editor.*

[26] See Part 11, Chap. 12. *Editor.*

[27] See Part 18, Chap. 14. *Editor.*

ity. The SGO-T activity was studied in 50 patients with coronary insufficiency whose ECGs showed evidence of ischemia as manifested by moderate to marked T-wave inversion sometimes associated with ST-segment changes but without Q-wave abnormalities. The SGO-T activity remained within normal limits in 34 of these patients despite the persistence of prolonged substernal pain. The SGO-T activity rose in 16 of these patients, suggesting acute heart muscle cell damage In 8 instances, pain had been present for 3 to 6 days before the SGO-T increased (Figs 10-6B, C).

ACUTE PERICARDITIS

The SGO-T was followed daily or oftener in 11 patients with unequivocal evidence of acute pericarditis of varying etiology; it remained within normal limits in 9 throughout the period of study Two exhibited a minor increase in SGO-T activity which was thought to be due to the presence of coexistent liver disease, due in one instance to infectious mononucleosis and in the other to leukemia

RHEUMATIC CARDITIS

The SGO-T activity in acute rheumatic fever without carditis was not elevated In some, but not all, patients with extensive rheumatic carditis, the SGO-T activity was increased It is to be noted that the administration of large doses of aspirin to children will also cause elevation of the SGO-T activity

PULMONARY INFARCTION

The SGO-T activity was followed during the course of pulmonary infarction in seven patients and remained at normal levels in all but one patient whose peak enzyme activity was 80 units

DISCUSSION

Although the spectrophotometric method employing the Beckman DU spectrophotometer is the most rapid and accurate method for the analysis of SGO-T, SGP-T, and SLD, the Bausche and Lomb spectrophotometer using Steinberg's modified technique (for SGO-T) is more economical and practical for smaller laboratories Colorimetric methods for all three enzymes have been devised and can be employed, using equipment already available in hospital laboratories The serum should be separated promptly from the red blood cells to avoid hemolysis and then stored at refrigerator temperature for not more than 4 days.

It is important to emphasize that, *unless serum is received within 3 days after the onset of infarction, the SGO-T activity cannot be relied upon as evidence of acute myocardial damage.*

It is worth reemphasizing that SGO-T activity is not increased as a result of infectious, degenerative, neoplastic, allergic, reactive, or congenital diseases or pregnancy unless there is associated acute damage of heart muscle, skeletal muscle, liver, kidney, or brain. No consistent correlation has been found between the SGO-T activity and the temperature, white blood count, sedimentation rate, or C-reactive protein.

Although marked elevations of SGO-T activity are seen in hepatitis of varying etiology and moderate increases occur in some patients with cirrhosis and obstructive jaundice, the clinical setting is such that there is rarely any confusion in the differential diagnosis with acute myocardial infarction Major surgery, when skeletal muscle is injured, is frequently followed by minimal to moderate increase in SGO-T, SGP-T, and SLD activity for 1 to 6 days which mimics that following acute myocardial infarction so that measurements of enzyme levels postoperatively do not constitute evidence for or against the presence of acute heart muscle cell injury. Metastatic cancer of the liver, moderately severe hemolytic crises, and mechanical injury to skeletal muscle are also associated with increased SGO-T activity

Experimental and clinical myocardial infarction is followed by characteristic changes in the activity in SGO-T, SLD, and SGP-T, with the peak activity occurring within 12 to 24 hr, falling to or toward normal within 2 to 5 days. The height and duration of elevated SGO-T activity are roughly proportional to the amount of myocardial necrosis.

The SGO-T activity increases proportionately more than the SLD or SGP-T following acute human myocardial infarction. The SLD activity can be measured by following the change of pyruvate to lactate which gives the maximum activity at physiologic pH or by measuring the changes from lactate to pyru-

ing an acute transmural myocardial infarction, the C-reactive protein is positive *after the third day. The test for C-reactive protein remains positive for as long as 3 to 7 weeks,* although it is usually elevated for only 2 weeks in the absence of complications Certainly the C-reactive protein returns to normal *before* the sedimentation rate in most instances The C-reactive protein has proved to be negative in patients with acute coronary insufficiency, whereas the sedimentation rate may be elevated in some instances. These tests have the advantage of simplicity and adaptability to most laboratories but must be evaluated carefully because of their lack of specificity and abnormal values in wide range of disease states.

The C-reactive protein is of particular value when blood samples are not obtained within the first 4 days following myocardial infarction, since the C-reactive protein remains positive much longer than does the SGO-T. The investigators who have studied the C-reactive protein have stated that this test may uncover small infarctions when the transaminase is normal. However, such findings must be carefully evaluated in the light of the nonspecificity of this reaction.

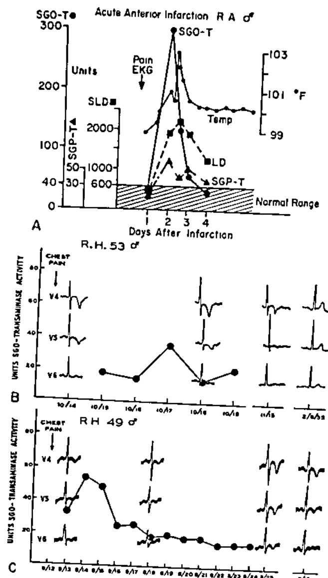


Fig. 10-6. A. The average changes in serum glutamic oxaloacetic transaminase, serum lactic dehydrogenase, and serum glutamic pyruvic transaminase activity in R.A. following acute transmural myocardial infarction B Marked, reversible ECG abnormalities in a patient with incapacitating precordial pain recurring every 30 min. from Oct 8 to Oct 20 The serum glutamic oxaloacetic transaminase remained normal. C. Serum glutamic oxaloacetic transaminase elevation in a man who had similar substernal pain and ECG changes

The SLD activity remained elevated 2 to 3 days longer than the SGP-T activity (Fig. 10-6A).

When left BBB obscured diagnostic electrocardiographic evidence of infarction in patients with severe chest pain, the SGO-T rose in some instances, indicating the presence of acute myocardial necrosis, but in other instances, no elevation occurred, suggesting the absence of infarction. The clinical course of these patients usually suggested that infarction was present when the transaminase was elevated. Four patients with electrocardiographic evidence compatible with *subendocardial infarction* were studied; in two, clear-cut increases in SGO-T activity occurred. The ECGs in the other two patients reverted toward normal when digitalis was withdrawn. When the SGO-T was elevated in patients with equivocal electrocardiographic changes, the usual treatment for myocardial infarction was instituted If the transaminase level was within normal limits, the patients were usually allowed out of bed within 1 week These findings have been corroborated elsewhere.

No correlation has been found between the SGO-T activity and the white blood count, the sedimentation rate, the presence or absence of shock, the absolute levels of the blood pressure, the presence of heart failure, the location of the infarction, or the use of anticoagulant drugs. *Peak activity above 350 units was associated with a marked increase in mortality rate.*

There was also a significant correlation between the SGO-T activity and the electrocardiographically estimated size of the infarct Higher enzyme levels were associated with more extensive electrocardiographic changes

The SGP-T activity increases proportionately less than SGO-T following injury to heart muscle but is higher following acute liver cell injury. The SLD activity, however, is relatively unaffected by liver cell injury but rises following heart muscle or skeletal muscle damage in parallel fashion to SGO-T.

PRECORDIAL PAIN. CORONARY INSUFFICIENCY

Myocardial ischemia in 15 dogs was produced by lifting a ligature placed 10 days previously under a coronary artery so as to cause marked T-wave and ST-segment changes but no Q-wave changes Four of these animals developed subendocardial infarction, and all had elevated SGO-T activity In the remaining 11 no microscopic evidence of heart muscle cell injury was found, and the SGO-T activity remained within normal limits in all but one dog despite the appearance of temporary electrocardiographic evidence of ischemia manifested by ST-segment and T-wave changes.

Precordial pain of variable duration has not been followed by an increase in SGO-T ac-

must determine from all the information at hand what type of heart disease is present. The nonspecific electrocardiographic changes may be helpful, however, when the diagnosis is in doubt, in pointing to abnormality of the heart

ATTACKS OF PRECORDIAL PAIN

Typical substernal pain after exertion is almost always caused by disease of the coronary arteries. The electrocardiographic findings sometimes provide important help in the diagnosis, but frequently the tracing is normal or shows nonspecific changes, in which event it is not helpful in diagnosing or excluding pain caused by coronary heart disease In some instances, the QRS deflections may be of low amplitude, or BBB may be present. Such electrocardiographic abnormalities are not usually found in patients with normal hearts and, while they occur in other forms of heart disease, they are so commonly associated with disease of the coronary arteries that their presence may help in the diagnosis of angina pectoris. Curves showing evidence of previous *myocardial* infarction are not uncommon in patients complaining of precordial pain and may be of great aid in the diagnosis.

Electrocardiograms are not often obtained during spontaneous attacks of substernal pain. In some instances, *displacement of the RS-T segment is recorded* The significance of slight deviations of the RS-T segment becomes more apparent upon comparison with tracings made shortly before or after the attack during which the record is obtained (Feil and Siegel). The displacement of the RS-T *segment* is usually *downward* In the leads showing depression of the RS-T segment, S waves may appear or, if present, become deeper. Transient changes resembling those of acute myocardial infarction may be recorded during *an attack of substernal* pain and disappear completely within a few minutes after cessation of the pain.

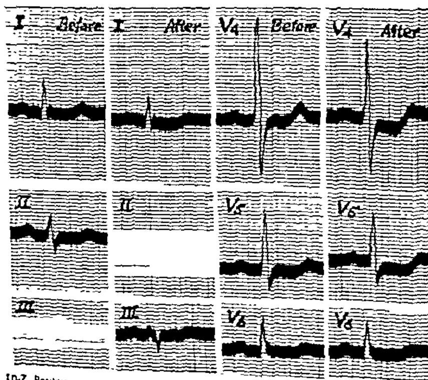


Fig 10-7 Positive *exercise* test in a 52-year-old physician *with a* duodenal ulcer and esophageal hiatus *hernia* and negative physical findings, who had atypical brief *episodes of pain across* the lower chest The *vertical* columns in order *show* standard leads I, II, and III *before* and after exercise and precordial leads V_4, V_5, and V_6 before and after *exercise* There is significant depression of the RS-T *segment* after exercise which is interpreted as *indicating* coronary insufficiency. The exercise *produced* shortness of breath and slight pain.

vate at pH 9. Preliminary reports suggest that the latter method gives results closely paralleling SGO-T, although the magnitude of SLD activity is five to ten times less by employing this method.

It is of interest that the SLD activity persists 2 to 3 days longer than SGO-T activity following acute myocardial infarction.

The SGO-T activity has proved particularly useful in deciding whether acute heart muscle cell damage has occurred when chest pain, like that seen with myocardial infarction, develops in patients with equivocal electrocardiographic changes. In such instances, if the SGO-T is carefully followed throughout the duration of pain and for 4 to 12 days thereafter, many patients may be saved weeks of invalidism, or anticoagulant therapy may be instituted to prevent impending infarction. Acute myocardial damage must be presumed to be present in patients with chest pain and equivocal electrocardiographic changes who have SGO-T elevation in the absence of known active liver disease Further study is needed to evaluate the usefulness of SLD in such situations, remembering that minimal hemolysis will increase SLD activity.

Agress and coworkers found that most of their patients with SGO-T activity above 300 units did not survive their acute myocardial infarction

The SGO-T activity will usually help distinguish acute pericarditis and pulmonary infarction from acute myocardial infarction, since SGO-T is uncommonly and only slightly and irregularly elevated following acute pericarditis and pulmonary infarction but rises promptly and follows a characteristic curve after acute myocardial infarction Further study is needed to evaluate the significance of SGO-T alterations in acute rheumatic carditis

The fact that infarcted heart muscle may contain one-fiftieth the GO-T, GP-T, and LD activity of normal heart muscle suggests that the increased levels in the serum following myocardial infarction result from the release of these enzymes from the damaged heart muscle cells in excess of that which the body can destroy or excrete (Fig 10-5A).

Deviations in the elevations of various enzymes following tissue damage are not solely explicable on the basis of a simple release into the blood stream, and other mechanism as yet unknown need to be elucidated.

Other enzymes present in heart muscle in high concentration may prove to be more significantly, more regularly elevated and remain so for a longer period of time than either SGO-T or SLD. It is obvious that continued study of other enzyme systems of many tissues or of tumors may provide useful information both with regard to diagnosis and changes in tissue cell metabolism.

The activity in the serum of *phosphohexose isomerase* was increased in 16 of 18 patients following acute myocardial infarction and that of *malic dehydrogenase* in 17 of 18. The measurement of the activity of malic dehydrogenase, however, was admitted by the authors not to be specific, and until the technique is stabilized and more results are available, the usefulness of these enzymes in the diagnosis of acute myocardial infarction will not be established.

NONSPECIFIC PHASE REACTANTS

The nonspecific phase reactants include the *erythrocyte sedimentation rate (ESR)*, the *C-reactive protein (CRP)*, and *fibrinogen*, and have all been studied as aids in the diagnosis of acute myocardial infarction. It has long been known that the sedimentation rate becomes elevated within 12 to 24 hr after acute myocardial infarction and may remain elevated for as long as 7 weeks. The increase in the sedimentation rate following infectious diseases or any disease associated with inflammation is a well-known fact. However, all these phase reactants are positive within the first 3 weeks in 90 to 98 per cent of patients sustaining acute myocardial infarction.

As intimated above, the C-reactive protein, sedimentation rate, and fibrinogen may be positive in infectious diseases as mild as an acute upper respiratory infection, in gastrointestinal diseases which are complicated by infection, in acute gout, in neoplastic diseases, as well as being altered by the mere presence of severe congestive heart failure. They are also strongly positive following pulmonary infarction, and of course in pericarditis, acute rheumatic fever, and rheumatoid arthritis and other collagen diseases.

In almost 100 per cent of patients sustain-

ward or S deflection, giving rise to a W-shaped complex. The QRS changes are maintained and are usually permanent.

The decline of the early *displacement of the RS-T segment* is accompanied and followed by *inversion of the T wave*, the terminal portion at first, which becomes quite pronounced near the margins of the infarct so as to produce a large, rather pointed, and *deeply inverted T wave*. This is a transient change which sometimes begins to regress within 24 hr.

Clinical Myocardial Infarction. PRECORDIAL LEADS In myocardial infarction in human beings, the electrocardiographic changes are usually, but not invariably, similar to those in the experimental animal and equally characteristic They evolve somewhat more slowly, however It is, of course, not possible to lead directly from the epicardial surface of the heart, but multiple leads from the surface of the chest have served very well as "semidirect" leads (Wilson et al , 1944) The electrodes on the chest wall are more distant from the heart than electrodes placed directly upon the exposed heart of the experimental animal For this reason, curves obtained by means of chest leads are dominated somewhat less by events occurring in that part of the heart which lies immediately beneath the exploring electrode and are influenced somewhat more by the activity of the remaining portions of the heart Nevertheless chest leads in man usually give records which closely resemble the curves obtained in the experimental animal by means of direct epicardial leads

In man the location of the infarct cannot be known in advance of taking the ECG, so that multiple chest leads are employed in order to examine the heart adequately The six precordial leads now in common use have been adopted as the most practical for everyday clinical electrocardiography They, along with the three standard leads and the three unipolar extremity leads, form the 12-lead ECG, which reaches its greatest usefulness in myocardial infarction If an infarct is present, in many but not all instances, it will be detected by this method Correlation of the clinical curves obtained in this manner with the postmortem findings and with experimental studies has established the basis for determining with considerable accuracy the location of the infarct from the form of the curve

When in man the anterior wall of the heart is infarcted, the changes which take place in the ventricular complexes of the precordial leads resemble those seen in direct leads from the infarcted area in the animal experiments Our knowledge regarding the earliest changes is incomplete because curves are rarely obtained immediately after the onset of the infarction. In a few instances, records have been obtained showing inversion of the T wave as the earliest change (Schlant et al.). This has been attributed to *ischemia.* There is early a pronounced *upward displacement of the RS-T junction and the RS-T segment.* Soon there appears a *prominent Q wave.* As the RS-T displacement declines, inversion of the terminal portion of the T wave occurs and progresses so that a large, rather sharply pointed, *deeply inverted T wave develops* The Q-T interval becomes prolonged. The deep inversion of the T wave persists long after the RS-T segment has returned to or near the base line. Eventually the sharp inversion of T becomes less pronounced, and in some instances, the T wave returns to its normal upright form, or nearly so The Q wave is prominent in relation to the other deflections of the QRS complex, it may become the sole deflection of this complex, or it may be followed by an R wave, or there may be a W-shaped complex. The QRS changes are usually permanent, rarely reverting to normal. The other changes evolve more slowly in man than in the experimental animal, displacement of the RS-T segment persisting for several days or a week and the deep inversion of the T waves for several weeks or months (Fig 10-8)

The alterations in the ventricular deflections are most pronounced and most characteristic when the precordial electrode is approximately *over the infarct.* When it is not over the infarct, the changes are absent or, at most, incomplete. When the characteristic changes are recorded in all or nearly all the precordial leads, it may be suspected that the infarct is large, and when they are limited to only a few of the precordial leads, it may be assumed that the infarct is small The T-wave changes are often recorded over a larger area than the characteristic QRS changes; they are commonly prominent in leads taken farther to the left than those which show the most conspicuous Q waves (Fig. 10-9).

Electrocardiography in coronary heart disease

PAUL S. BARKER

By means of electrocardiography important contributions have been made to the clinical recognition and understanding of coronary heart disease. However, it must be emphasized that electrocardiography is only one of several methods for examining the heart and that *electrocardiograms do not record changes in the coronary arteries:* they give evidence of coronary artery disease only as it causes ischemia, injury, or necrosis of the myocardium or alters the cardiac rhythm or conduction *The electrocardiographic findings, therefore, are not specific for coronary disease* Alterations in rhythm or in conduction are commonly due to other causes. Ischemia, injury, and necrosis are usually the result of narrowing or obstruction of a coronary artery, but are sometimes due to other causes. The ECG is best interpreted as showing a disturbance in rhythm or in conduction or as giving evidence of ischemia, injury, or necrosis, the sum of the clinical findings then determines whether or not the changes are caused by coronary artery disease In patients of middle age and beyond, and without any other apparent explanation, such changes are nearly always of coronary origin, but they have been observed in neoplastic involvement, trauma, inflammatory disease, and other conditions of the heart The diagnosis of coronary disease should be a clinical and not an electrocardiographic diagnosis. The only exception to this general rule is the diagnosis of myocardial infarction which may be made on electrocardiographic findings alone, when they are characteristic.

It is important to remember that the ECG *is sometimes normal in the presence of severe and extensive coronary sclerosis.* The coronary disease may be pronounced, but if it does not affect the rhythm or conduction, or cause ischemia, injury, or necrosis, it will not alter the ECG. Indeed, myocardial infarction not favorably located with respect to the electrocardiographic leads may cause little change in the ECG. A normal ECG does not necessarily mean a normal heart. Conversely, minor peculiarities of the ECG, the meanings of which, if any, are not yet known, do not of themselves justify a diagnosis of heart disease.

CORONARY SCLEROSIS

The alterations in rhythm or in conduction and evidence of preponderant hypertrophy of the left ventricle, both common in coronary heart disease, are observed in other conditions as well. They are not specific for coronary heart disease and will not be described It has been shown that *inversion of the T waves accompanies myocardial ischemia,* but T-wave inversion occurs in other conditions as well, in which ischemia is not present. The common type of abnormal T-wave inversion is not specific for any particular kind of heart disease, and although it is common enough in coronary heart disease, *it is best interpreted merely as indicating myocardial changes.* The clinician

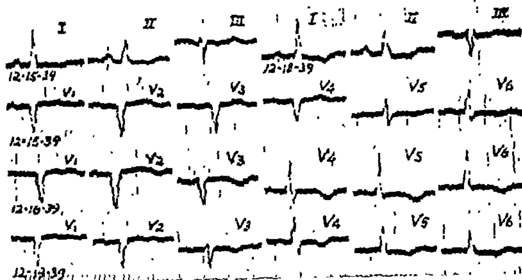


Fig. 10-9. Antero-septal infarction. Electrocardiograms of a 67-year-old physician who had typical precordial pain for several weeks prior to the onset of persistent pain on Dec 15, 1939. The first ECG was taken a few hours after the onset of the pain. The standard leads I and II show slight inversion of the T waves which has become somewhat more pronounced by Dec. 18, but this is the only change in the standard leads which might suggest myocardial infarction. Changes in the QRS complexes are notably absent. The precordial leads are characterized by prominent QS deflections and progressive changes in the T waves, characteristic of recent myocardial infarction. The patient died suddenly on Dec 20, 1939. Autopsy showed a small old infarct high on the anterior wall of the left ventricle and a small area of fresh infarction just below the old scar. There were much smaller old and recent infarcts on the posterior wall of the left ventricle. There was advanced coronary atherosclerosis with almost complete sclerotic occlusion of the anterior descending branch of the left coronary artery and fresh thrombotic occlusion of the posterior descending branch of the right coronary artery.

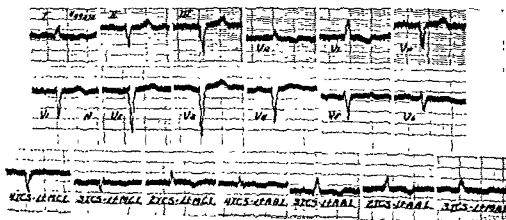


Fig. 10-10. High lateral infarction. Electrocardiograms of a 57-year-old man with intermittent claudication, varicose veins, and thrombophlebitis, but no cardiac symptoms. The QRS complex is small in lead I, the S waves are deep in leads II and III, and the T waves are inverted in leads I and VL. The precordial curves are unusual in showing small R waves and prominent S deflections in all leads. Myocardial infarction was suspected, but conclusive evidence was lacking. Special leads from points high in the left midclavicular line and left anterior axillary line show prominent Q waves and inverted T waves interpreted to indicate an old high lateral infarct. There was no autopsy.

Although great reliance must be placed upon subjective symptoms, and even though they may be atypical and may be simulated by other conditions and despite the absence of objective findings, the diagnosis of coronary disease can ordinarily be made with considerable accuracy. Occasionally, however, there are patients in whom the diagnosis is not clear. The problem is whether there is serious coronary artery disease or no organic disease of the heart. When, for special reasons, it seems sufficiently important to establish a diagnosis to justify the slight risk involved, an *exercise test* for coronary insufficiency may be performed. Electrocardiograms made before and immediately after the test exercise are compared. The test exercise may consist of walking briskly or climbing stairs or the "two-step test" (Master).

The two-step test of Master affords a more precise measure of the effort expended by the patient. It has been useful in studying the effects of various forms of treatment for coronary pain (angina pectoris) as well as in the diagnosis of coronary insufficiency. The exercise is intended to put the heart under a standard degree of stress. It should be terminated at once at the onset of precordial pain or pronounced breathlessness. Comparable stress may be provided by having the patient breathe an oxygen-poor mixture of gas (10 per cent oxygen). The test is regarded as positive for coronary insufficiency if definite displacement of the RS-T segment is produced (Fig 10-7). The test has its limitations and is not entirely reliable, some patients with important degrees of coronary artery disease may respond normally to the exercise, while others with no coronary disease may give a positive response. Because every attack of coronary pain offers a threat to the life of the sufferer, this test should not be employed indiscriminately, but only in those instances in which the risk, however small, seems for special reasons to be justified.

MYOCARDIAL INFARCTION

The most important contribution of electrocardiography to clinical medicine is in the diagnosis of myocardial infarction. Myocardial infarction is almost invariably caused by coronary artery disease. The alterations in the ECG which accompany myocardial infarction are caused by the changes in the cardiac muscle supplied by the diseased artery rather than by the changes in the artery itself. It is, therefore, appropriate to ascribe the electrocardiographic abnormalities to myocardial infarction rather than to coronary thrombosis or coronary occlusion.

Experimental Myocardial Infarction. Experimental infarction may be produced in the experimental animal by ligating a large branch of a coronary artery, and the resulting electrocardiographic changes may be studied in the standard leads (Smith) and by means of direct leads from the exposed heart (Wilson et al, 1934, 1935, and 1938). Records obtained by leading directly from the epicardial surface of a transmural infarct show characteristic changes. Within 3 or 4 sec, *inversion of previously upright T waves appears*, or previously inverted T waves become more deeply inverted. This change reaches its height in 20 to 25 sec. It is attributed to *ischemia* of the underlying muscle (Bayley et al).

Within 1 or 2 min, *upward displacement of the RS-T junction and of the RS-T segment* makes its appearance. This displacement increases in magnitude and reaches its height in a few minutes, it begins to regress after about 1 hr and gradually disappears in 10 to 15 hr. The shift in the RS-T segment may be so pronounced that the entire ventricular complex becomes monophasic or nearly so. The RS-T displacement is attributed to *injury* to the muscle beneath the electrode.

Within a few minutes after ligation of the coronary artery, *prominent Q waves appear.* Over the central part of the infarct (where it is transmural), the initial ventricular complex may be one large QS deflection. The prominent Q wave is attributed to the *death or necrosis, or at least the nonfunctioning, of the infarcted muscle.* Instead of contributing to the QRS complex, the nonfunctioning muscle conducts to the electrode placed upon its epicardial surface the potential changes of the remainder of the heart, most of which follow vectors that are oriented away from the electrode. In essence, the infarcted muscle conducts to the epicardial electrode the variations of potential of the cavity of the ventricle. The curve obtained by leading from the epicardial surface of a transmural infarct may be reproduced by leading from the cavity of the ventricle (Wilson). Over the periphery of the infarct, or where it is subendocardial rather than transmural, the initial Q wave is somewhat smaller and is followed by an upward, or R, deflection. The R deflection is caused by the depolarization, in the wall beneath the exploring electrode, of muscle which is still capable of responding. The R deflection may in turn be followed by a down-

endocardial layers of ventricular muscle, yield instead of deep QS deflections *somewhat* smaller Q waves *followed* by upward R deflections (Fig. 10-8, V_3, curves of August 11 and September 9, 1943) The Q waves *represent* the cavity potential transmitted to the precordial electrode, while the R waves record subsequent activation of healthy subepicardial muscle overlying the infarct. In *acute subendocardial infarction*, the RS-T segment may be displaced in either direction

Infarction of the posterior wall of the heart often does not cause significant *changes in* the usual precordial leads. When changes are observed, they usually are not pronounced Soon after *the onset* of the infarction, *there* may be *downward displacement of the* RS-T *junction and the* RS-T *segment*, usually not so great as the upward displacement which occurs in anterior infarction. Later, *the T waves may become unusually tall* and rather *sharply pointed*, corresponding to the deep and sharp inversion of anterior infarction, but they do not differ strikingly *from the normal* upright T waves (Fig. 10-11). Posterior infarction does not give rise to any characteristic alteration of *the QRS complex in the precordial* leads.

When the exploring electrode is placed over *the lower chest posteriorly*, characteristic changes of infarction *may* be recorded in some cases (Figs. 10-13 and 10-14). These resemble the changes observed in the precordial leads in *anterior myocardial infarction*, but the deflections are smaller in amplitude because of the greater distance of the exploring electrode *from the heart. In some instances of posterior* characteristic alterations may be

leads, it is possible to place *the exploring* electrode close to the posterior *surface of the* ventricles, and this has been useful in a few rare instances in establishing the diagnosis, not otherwise clear, of old posterior infarction. Because they may be quite disturbing to the patient, the use of esophageal leads is not rec-

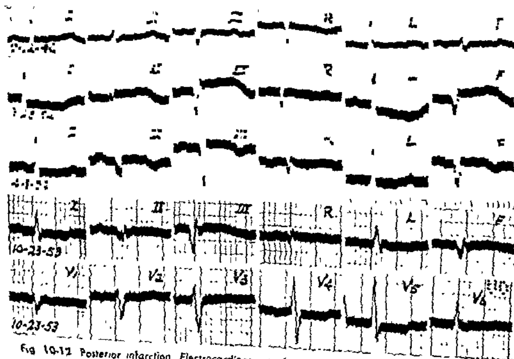


Fig 10-12 Posterior infarction Electrocardiograms of a man who was 81 years of age at the onset of myocardial infarction on the morning of Mar 28, 1952, showing the progressive changes of posterior infarction The curves of Oct 23, 1953, show intraventricular block of uncertain type with the Q waves of leads II, and III, and aVF retained. The patient died June 22, 1954. Autopsy showed hypertrophy of the left ventricle, old infarction of the posterior wall of the left ventricle, and an organizing thrombus occluding the right coronary artery.

The characteristic changes of myocardial infarction are sometimes limited to the second, third, and fourth precordial leads, and under these circumstances, the standard leads give no evidence of infarction (Fig. 10-9). This is the case when the infarct is confined to the anterior and septal region of the heart without involving its lateral portions, the *anteroseptal infarct*. In this circumstance, the alterations in electrical forces produced by the infarct are in the anteroposterior axis with little, if any, projection on the frontal plane. As a result, the potential variations in the frontal plane are not altered appreciably, and it is these which are recorded in the standard leads. Commonly, however, the fourth, fifth, and sixth precordial leads show the typical alterations. This is observed when the infarction of the anterior wall involves the left lateral wall as well, so that the potentials of the left arm are altered, with resulting changes in standard lead I (*anterolateral infarct*).

In rare instances, a small infarct located unusually *high* in the anterior or lateral wall of the heart will not give rise to characteristic alterations in the usual precordial leads. In such cases, special leads with the exploring electrode placed one or two interspaces higher on the left chest anteriorly or in the left axillary region may yield curves showing the typical changes of infarction (Fig 10-10).

Chest leads over the margins of an infarct, where the lesion is subendocardial rather than transmural, or over infarcts limited to the sub-



Fig. 10-8. Anterior myocardial infarction showing progressive changes Electrocardiograms of a woman who was 40 years of age when myocardial infarction occurred on Aug 6, 1943. The first record was obtained 6 hr later and the second curve 27 hr after the onset. They show inversion of the T waves in leads I, aVL, and V_1, V_2, V_3, V_4, and V_5, which may represent the first change of infarction due to ischemia In the records of Aug. 9 and 11, 1943, there is upward displacement of the RS-T segment in these leads and the T waves are no longer inverted except in V_1 Aug 11 Conspicuous Q waves were present in leads I and aVL on Aug 9, and prominent QS deflections in V_1, V_2, V_3, and V_4 on Aug. 11. As the RS-T segment returns to the base line, Sept 9, 1943, the characteristic deep inversion of the T waves appears and the Q waves persist In later curves, taken on the same patient shown in Fig. 10-15, the inversion of the T waves becomes less pronounced.

endocardial layers of ventricular muscle, yield instead of deep QS deflections somewhat smaller Q waves followed by upward R deflections (Fig 10-8, V_5, curves of August 11 and September 9, 1943) The Q waves represent the cavity potential transmitted to the precordial electrode, while the R waves record subsequent activation of healthy subepicardial muscle overlying the infarct. In *acute subendocardial infarction*, the RS-T segment may be displaced in either direction

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leads, it is possible to place the exploring electrode close to the posterior surface of the ventricles, and this has been useful in a few rare instances in establishing the diagnosis, not otherwise clear, of old posterior infarction. Because they may be quite disturbing to the patient, the use of esophageal leads is not rec-

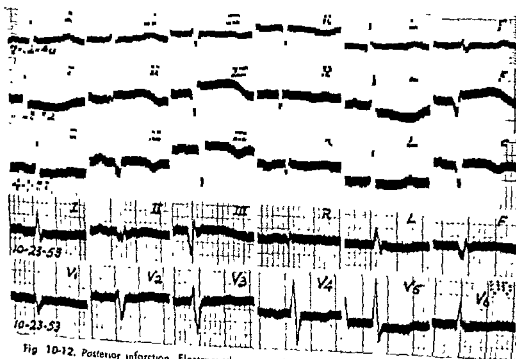


Fig 10-12. *Posterior infarction Electrocardiograms* of a man who was 81 years of age at the onset of myocardial infarction on the morning of Mar 28, 1952, showing the progressive changes of posterior infarction The curves of Oct. 23, 1953, show intraventricular block of uncertain type with the Q waves of leads II, and III, and aVF retained The patient died June 22, 1954 Autopsy showed hypertrophy of the left ventricle, old infarction of the posterior wall of the left ventricle, and an organizing thrombus occluding the right coronary artery.

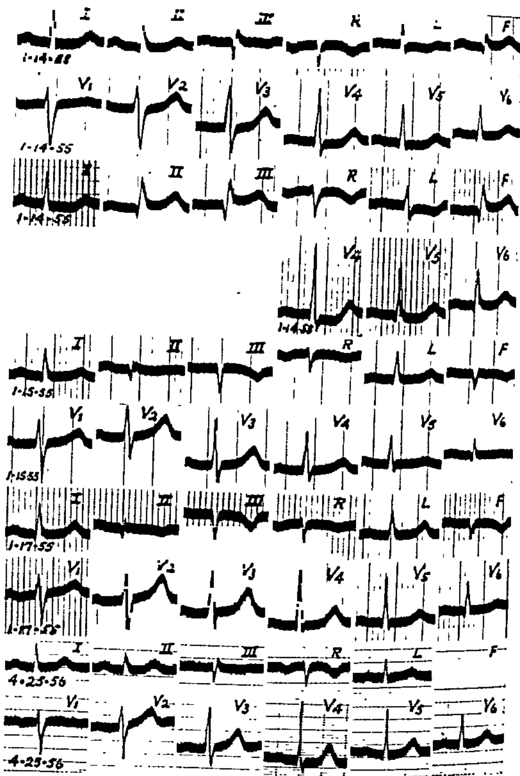


Fig. 10-11. Posterior myocardial infarction showing progressive changes. Electrocardiograms of a 54-year-old physician who had the onset of myocardial infarction on Jan. 14, 1955. The first record, obtained 4 hr after the onset, shows prominent Q waves in leads III and aVF and small Q waves in leads I and II and V_4, V_5, and V_6, all of doubtful significance. In the second curve, made a few hours later, the Q deflections are conspicuous in leads II, III and aVF, somewhat larger in V_6, and quite small in lead I and V_4 and V_5, and the RS-T segment is elevated in leads II, III, and aVF and depressed in aVL and V_4. On the following day the RS-T segment had returned to the base line, inversion of the T waves appeared in leads III and aVF and the Q waves persisted except in V_4. On Jan 17, 1955, the T wave inversion was more pronounced in leads II, III, and aVF, and the T waves in V_1, V_2, V_3, and V_4 had become taller. These changes took place with more than the usual rapidity. Subsequent records showed a gradual return to a more nearly normal appearance and by Apr. 25, 1956, the only trace of the previous infarction is the prominent Q waves in leads III and aVF.

served in the unipolar lead from the left leg and in standard leads II and III and are lacking in the precordial leads, there is *infarction of the posterior wall* of the heart. If, in addition, the sixth precordial lead shows similar changes, the *infarct is posterolateral* in location.

Atypical Electrocardiograms. Occasionally, however, there are discrepancies, and the alterations in the ECG are not consistent. The changes in the standard leads may be the same in all three leads instead of being reciprocal in leads I and III as is usually the case. Rarely, the standard leads are of the Q_3T_3

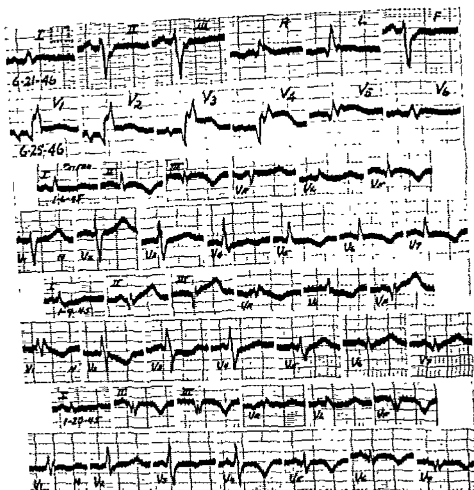


Fig 10-13. Myocardial infarction and right BBB Electrocardiograms of a 65-year-old man who experienced myocardial infarction on June 14, 1946, are shown in the first two curves. The characteristic changes of anterior infarction are retained in the presence of right BBB. Death occurred on June 29, 1946 Autopsy showed occlusion of the left coronary artery and massive infarction of the anterior wall of the left ventricle and the interventricular septum

The remaining curves are those of a 70-year-old woman who suffered myocardial infarction on Jan 3, 1945 The typical changes of posterior infarction are not obliterated by the development of right BBB The presence of Q waves in V_6 and V_7, the latter from the posterior axillary line, and of inverted T waves in leads from the left side of the precordium indicates that the infarct is posterolateral January 6, 1945, signs of posterolateral infarction January 9, 1945, signs of fresh infarction in leads II, III, VF, V_6, and V_7, accompanying a return of the pain. January 20, 1945, progression as expected and QRS changes more distinct in V_6 and V_7. There has been extension of the infarct. The patient died on Jan 29, 1945. Autopsy showed recent infarction of the posterior and posterolateral walls of the left ventricle resulting from recent thrombotic occlusion of the right coronary artery which supplied these portions of the left ventricle in an anomalous manner

type while the precordial leads are characteristic of anterior infarction. Other peculiarities sometimes occur. A number of factors may contribute to the occurrence of these discrepancies.

The *form* of the ECG is influenced to a considerable degree by the position of the heart or of its mean electrical axis, and when this is unusual, it may lead to confusing peculiarities in the ventricular complex. Any abnormalities of the ECG which may have been present before myocardial infarction occurred must have an important influence in determining the form which it will have afterward. Although right BBB modifies the form of the curve in myocardial infarction, it does not obscure the changes resulting from the infarction, and they may still be recognized (Figs. 10-13 and 10-16). *Left BBB, on the other hand, obscures the characteristic changes of infarction* (Fig 10-14), *the Q waves of infarction representing the negative potential of the left ventricular cavity, whereas in left BBB, the potential of the left ventricular cavity is positive initially.*

The presence of more than one infarct may account for some of the discrepancies. Since the Q waves of infarction are usually permanent and the changes in the RS-T segment and in the T waves are commonly transient, the QRS changes of an old infarct may be combined with displacement of the RS-T segment or inversion of the T waves due to a recent infarct. An anterior infarct may determine the form of the precordial leads, while a posterior infarct may control the form of the standard leads (Fig 10-15). Two infarcts, both old or both recent, may partially neutralize each other so far as the standard leads are concerned.

Occasionally, the displacement of the RS-T segment, instead of declining in the usual manner, persists for many months. This is usually associated with an aneurysm of the ventricle in the scar of a previous infarct (Schlichter et al). Commonly, there are Q waves and terminal inversion of the T waves as well (Fig. 10-16). A single ECG suggests acute or recent myocardial infarction, but serial curves show that the pattern is fixed and does not change progressively as in acute infarction. The explanation of this curious phenomenon is not known.

DIFFERENTIAL DIAGNOSIS

Not uncommonly, some of the electrocardiographic features of myocardial infarction are encountered in the absence of heart disease or in the presence of other types of heart disease. Large Q deflections and inverted T waves in lead III only are common in individuals with *normal hearts having an electrical axis in or near the horizontal position*, as in obesity, such curves are not diagnostic of myocardial infarction. Pronounced *hypertrophy of the right ventricle* commonly gives rise to large Q deflections in leads II and III, and sometimes in lead I, too, but in such curves the T waves are rarely inverted so that they are not likely to lead to difficulty. Preponderant hypertrophy of the left ventricle is sometimes accompanied by large Q or QS deflections in the first and second precordial leads, but the T waves are upright (Master et al).

In *pulmonary embolism*, there are sometimes prominent Q waves and inverted T deflections in lead III while the RS-T segment is displaced downward in lead I and the T waves are inverted in the first three pre-

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and V_4, this is consistent with left BBB. Autopsy showed old and recent infarction of much of the left ventricle.

The last four rows show the curves of a man who was 56 years of age when he suffered myocardial infarction on Apr 11, 1952. The record of May 2, 1952, is characteristic of recent posterolateral infarction. Attention is directed to the downward displacement of the RS-T segment in V_5 and to the small Q waves and inverted T waves in V_6 and V_7, the latter from the posterior axillary line. On Mar 19, 1957, auricular fibrillation and left BBB were present. The ventricular deflections are characteristic of left BBB and not of myocardial infarction. The patient died soon after the last curve was obtained. Autopsy showed pronounced coronary atherosclerosis and old posteroseptal myocardial infarction. The degree to which the infarction of the septum may have modified the deflections in leads II and III and aVF is probably minor. Complexes like these are observed in left BBB without myocardial infarction.

ommended in acute myocardial infarction. It should be kept in mind that myocardial infarction involves the left ventricle chiefly and that the so-called posterior wall of the left ventricle is actually oriented toward the diaphragm and more inferiorly than posteriorly.

UNIPOLAR EXTREMITY LEADS. As mentioned previously, infarction of the anterior wall of the heart commonly involves its lateral wall as well, and infarction of the posterior wall presents toward the diaphragm inferiorly. The former is revealed by the characteristic changes in the usual precordial leads over the left anterolateral border of the heart, while the latter is demonstrated by the typical alterations in special leads over the lower chest posteriorly or over the upper abdomen Thus anterior infarcts are commonly oriented toward the left arm as well as anteriorly and therefore alter the potentials of the left arm, while posterior infarcts are oriented inferiorly and thus modify the left leg potentials.

In most instances of anterior infarction, Q is prominent, displacement of the RS-T segment is upward, and the T waves become deeply inverted in the unipolar lead from the left arm (Fig. 10-8). These changes occur almost invariably in the unipolar lead from the left leg when the posterior wall of the heart is infarcted (Figs. 10-11 and 10-12). These alterations in the potentials of the extremities are the basis for the characteristic changes in the standard leads

STANDARD LEADS. When Q is prominent, RS-T is displaced upward or T is inverted in the left arm potentials, these features will be recorded in standard lead I. When these changes occur in the left leg potentials, they will be reproduced in standard lead III and, to a lesser degree, in standard lead II (Figs 10-11 and 10-12) Thus two well-defined types of standard ECGs are seen in myocardial infarction (Parkinson and Bedford, 1927–29, Barnes and Whitten, Wilson et al., 1933). They have been called the Q_1T_1 type and the Q_3T_3 type, respectively

In the Q_1T_1 *type of anterior infarction* (Fig 10-8) the QRS changes are characterized in lead I by a prominent and often broad Q wave which is sometimes the sole initial deflection, but is nearly always followed by an R wave which may be followed in turn by an S wave The QRS deflections in lead I are usually of small amplitude, the largest rarely exceeding 0 5 mv. In leads II and III, the initial ventricular deflection is an R wave, corresponding in time to the Q wave of lead I but usually of larger amplitude. This initial R wave may be the chief deflection of the QRS complex, but it is usually followed by an S wave which may be considerably larger than the R deflection. Occasionally, there is a definite Q wave in lead II as well as in lead I. Occasionally, the QRS complexes are small in all three leads, and other peculiarities are sometimes seen. For a few days after the onset of the infarction, the RS-T segment is displaced upward in lead I and downward in lead III. The decline of the RS-T displacement is accompanied and followed by the appearance of deeply inverted and rather sharply pointed T waves in lead I and of similar but sharply upright T waves in lead III. The RS-T and T-wave changes in lead II commonly resemble those of lead III, but sometimes they are more like those of lead I (Pardee).

Electrocardiograms of the Q_3T_3 *type of posterior infarction* (Figs. 10-11 and 10-12) are characterized by prominent Q waves in leads II and III. In lead III, Q is usually of large amplitude, and it may be the sole deflection of the QRS complex In lead II, Q is smaller and may, indeed, be quite small. In lead I, the first deflection is almost always an R wave, but occasionally a small Q wave is seen. For several days after the onset of the infarct (Fig 10-12), the RS-T segment is displaced upward in leads II and III and downward in lead I As the RS-T displacement declines, the sharp, deep inversion of the T wave makes its appearance in lead III, while the T wave of lead I is upright and somewhat smaller than that of lead III

Location of the Infarct. It is apparent from the previous considerations that the location of the infarct determines the particular characteristics of the ECG. It follows that the particular features of the ECG permit a fairly accurate prediction as to the location of the infarct. The presence of prominent Q waves with early upward displacement of the RS-T segment and later deep inversion of the T waves in the precordial leads, the unipolar lead from the left arm, and standard lead I indicates *infarction of the anterior wall of the heart* When the changes are conspicuous in the fifth and sixth chest leads, we may recognize *anterolateral infarction*. When the characteristic changes are confined to the second and third precordial leads and are lacking in the unipolar extremity leads and in the standard leads, the infarct is *anteroseptal* in location When these typical alterations are ob-

segment in all three standard leads and in the precordial leads without displacing the RS-T junction significantly. Inverted T waves are common in various types of *myocardial disease*. Inversion of the T waves may be caused by hysterical *hyperventilation*, and the combination of apparent dyspnea and an abnormal ECG may suggest serious heart disease, but the QRS complex is not altered significantly.

It is thus apparent that there is no single reliable criterion for the electrocardiographic diagnosis of myocardial infarction. Only when the characteristic changes of the types described are present in both the initial and the final ventricular deflections can the diagnosis be made with confidence from a single ECG. Not infrequently, however, the electrocardiographic changes are incomplete. Characteristic T-wave changes may not be accompanied by QRS changes and vice versa, or small bizarre deflections of intraventricular block may obscure the typical alterations. In such instances, the ECG may still be of great help in the diagnosis by providing evidence of abnormality of the heart. A knowledge of the symptoms or of the circumstances under which the record was obtained may aid considerably in arriving at the correct interpretation. In acute or recent infarction, the greatest help may come from obtaining a series of curves at intervals of a day or two, which may show *progressive changes* of the type expected in myocardial infarction. When the clinical findings *suggest acute myocardial infarction* but the ECG is not confirmatory, it is imperative that additional curves be obtained at suitable intervals.

In myocardial infarction, various nonspecific abnormalities of the ECG are common, abnormalities which may be due to myocardial infarction but which occur in other forms of myocardial disease as well. Some are important because, although the form of the curve may be altered, the diagnostic features of myocardial infarction are retained, if they are recognized, they may aid in the diagnosis. Others are important because they obscure the diagnostic features of infarction, and such curves are of no value in excluding myocar-

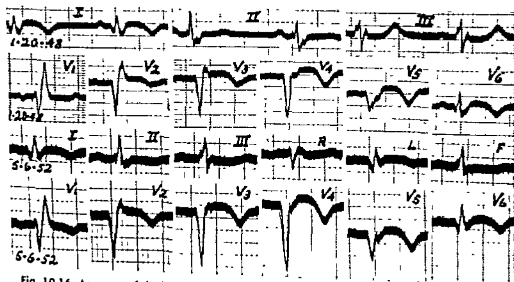


Fig 10-16 Aneurysm of the left ventricle. Electrocardiograms of a hypertensive businessman who was 55 years of age when myocardial infarction occurred on July 8, 1947. The record of Jan. 20, 1948, is characteristic of extensive anterior infarction, the signs of which are retained in the presence of right BBB. The RS-T segment is elevated in V_2, V_3, V_4, and V_5 6 months after the infarction. On Apr 29, 1952, the physical signs of aneurysm of the left ventricle were first detected, and its presence was confirmed by *x-ray*. The curve of May 6, 1952, is similar to that of Jan 20, 1948, showing the signs characteristic of extensive anterior infarction and right BBB, and the same upward displacement of the RS-T segment and deep terminal inversion of the T waves in V_2, V_3, V_4, and V_5. The curve suggests recent infarction, but comparison with the previous record shows that the changes are fixed or persistent.

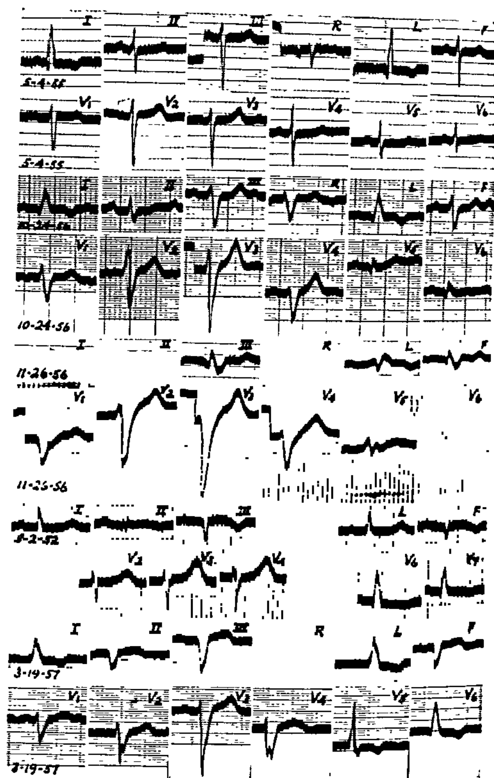


Fig.10-14. Myocardial infarction and left BBB. The first six rows show the records of a woman who was 44 years of age in 1953 when she developed precordial pain. There was no clear history of myocardial infarction The record of May 4, 1955, was reported as suggesting high lateral infarction although the findings were incomplete. In lead I and the lead from the left arm the T waves are inverted, and although Q waves are present, they are relatively small and the R waves are quite tall, and while Q waves are not present in the chest leads, the R waves of V_3 are relatively small The curve of Oct. 24, 1956, shows evidence of anterolateral infarction of indeterminate age and intraventricular block, possibly peri-infarction block. On this date leads I and aVL show significant Q waves and terminal inversion of the T waves, the R waves are small in V_4, and Q waves are prominent in V_5 and V_6. On Nov. 26, 1956, the appearance of complete left BBB has abolished the signs of myocardial infarction. Q waves are no longer present in leads I, aVL, V_5 and V_6, and although the R waves are small in V_3

minor and not at all characteristic of infarction

The curve shown in Fig 10-17 was interpreted as abnormal, showing rather small R waves in V_3 and flat T waves in lead I and inverted T waves in leads II and III and V_4, V_5, and V_6. It was obtained in a 47-year-old man who had edema and ascites for 2 years but no dyspnea or chest pain. The finding at autopsy of sclerotic occlusion of the anterior descending branch of the left coronary artery and old and recent infarction of the septum and anterior wall of the left ventricle was unexpected

SUMMARY

The ECG may be normal in the presence of advanced coronary artery disease if the heart muscle is not seriously affected Commonly, however, it shows abnormalities such as arrhythmias, conduction defects, or inversion of T waves. Although these abnormalities are not specific for coronary heart disease, they may be helpful in indicating abnormality of the heart Evidence of coronary narrowing may be provided by displacement of the RS-T segment following a standard exercise test. Similar changes have been observed during attacks of precordial pain.

Electrocardiograms reach their greatest usefulness in myocardial infarction in which characteristic changes are usually produced. The prominent Q waves and the upward displacement of the RS-T segment and the later striking inversion of the T waves are so characteristic that, when they are recorded, infarction is almost invariably present. Indeed, not only may the presence of myocardial infarction be recognized, but also its location may be predicted with a fair degree of assurance. Occasionally, however, the typical changes are not observed, but serial curves may undergo progressive alterations of diagnostic significance Because of the tendency of the ECG to revert in time to a more nearly normal form, old myocardial infarcts may not be recognized.

cordial leads. Slight displacement of the RS-T segment, of 1 mm or a little more, is sometimes seen in normal ECGs and in the absence of heart disease. Somewhat greater and usually permanent displacement is common in the presence of *pronounced axis deviation* or *BBB*. Transient RS-T displacement may be seen in various *acute febrile illnesses*, such as pneumonia and acute rheumatic fever, and the direction of the displacement is usually the same in all three standard leads as contrasted with myocardial infarction in which the shift is in opposite directions in leads I and III.

In *acute pericarditis*, the RS-T segment is commonly elevated in some or all of the three standard leads and sometimes in the precordial leads as well, lasting several days or a week or longer; the T waves become flattened and, in a few weeks inverted, and in a few months return to normal The curves of acute pericarditis differ from those of acute myocardial infarction in the absence of QRS changes, in the concordant character of the RS-T displacement, and in the failure of the T waves to become deeply and sharply inverted.

Trauma to the heart, whether penetrating or nonpenetrating, may cause displacement of the RS-T segment and alterations of the T waves. Large doses of *digitalis* commonly cause downward displacement of the RS-T

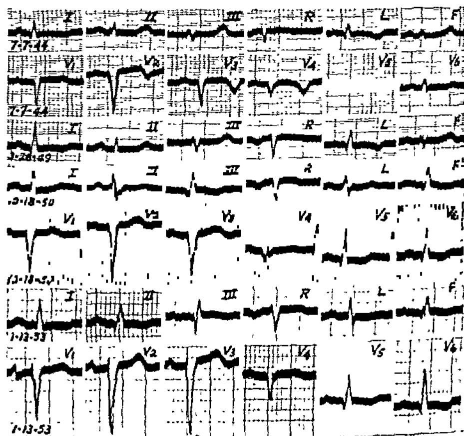


Fig. 10-15. Anterior infarction followed by posterior infarction. These are additional ECGs of the patient whose curves of anterior infarction are shown in Fig. 10-8 The records of July 7, 1944, and of Mar. 28, 1949, show further progression of the changes of anterior infarction. In December, 1949, she suffered a second myocardial infarction The curve of Oct. 18, 1950, shows the prominent Q waves and inverted T waves in leads II, III, aVF, characteristic of posterior infarction, while the prominent Q waves of anterior infarction are preserved in the precordial leads. Later these prominent Q waves disappear from the leads over the right side of the precordium but are retained in the leads from the left side of the precordium, as shown in the record of Jan. 13, 1953 The patient died suddenly on May 22, 1957. Autopsy showed severe coronary atherosclerosis with a recent thrombus occluding the anterior descending branch of the left coronary artery, which was probably the cause of death In addition there was old anterior myocardial infarction with slight aneurysmal dilatation, old posterior myocardial infarction, and recent septal infarction

the author able to observe both the left and the right coronary arteries over all their lengths, as continuous ribbons. In all these cases, the calcifications have movements which are synchronous with those of the heart. The validity of these images has been confirmed by postmortem studies. It is necessary to differentiate these shadows from those of calcifications of the costal cartilages or the bronchial walls An easy differentiation is that from calcification of lymph nodes and from the interlobar scissures. The calcifications of the cardiac valves have different form, location, and movements The pericardial calcifications before their final stage might lead to confusion, especially because they are frequently found in the same location as the coronary arteries The roentgenologic observation of coronary calcifications is infrequent, they are found only if they are searched for systematically. They are more common in aged persons (3 5 per cent of the cases according to Pyke and Symons) with a high degree of calcification and a small heart in a thin chest It is remarkable that these images have been observed even in old persons who had neither precordial pain nor serious electrocardiographic alterations.

Coronary Visualization. The postmortem visualization of the coronary arteries in isolated hearts has been obtained by numerous authors for anatomic or pathologic studies (Mouchet, Heim de Balsac, Schlesinger) The roentgenologic topography and the existence of anastomoses between the various vessels have thus been established (Heim de Balsac) (Fig 10-18) In addition, the alterations of the coronary arteries (tortuosity, sinuosity, spiral shape, irregularity of contour, variations of caliber, local narrowing, double contour, vascular obstruction, ischemic areas, etc) and the modalities of the collateral circulation have been studied These investigations have a remarkable value because they are the foundation for studies on the mechanism of coronary heart disease and on surgical attempts at revascularization of the myocardium A correlation between areas of ischemia revealed by the ECG and the structural changes of the coronary system has also been attempted (Pizano, Myers) However, in spite of the importance and number of these studies, this field of investigation has not been completely explored and further studies are necessary. The postmortem visualization of the coronary arteries has been realized in situ by the author with a special technique.

The dead body is suspended upright behind a fluoroscopic screen. The lungs are distended in order to obtain their transparency and push the diaphragm in its normal position. In this way, the heart appears exactly as in the living subjects An injection of barium sulfate through a carotid artery then fills the aorta and its branches, including the coronary arteries. The fluoroscopic observation is completed by x-ray films in different projections, which show the situation of the coronary system.

The coronary arteries emerging from the sinus of Vasalva are very high at the junction of the heart to the large vessels of the base In the PA and RAO positions, the *left coronary artery* goes toward the middle arch and branches off. The anterior descending branch descends over the ventricular mass while the left circumflex artery is situated behind it

The *right coronary artery* describes a curve which overlaps the shadow of the spine and is placed before it in the RAO position. In the LAO position, the two coronary arteries surround the cardiac mass and follow its borders more or less In *lateral projections,* both vessels are anterior and describe a loop which shows their ramifications with a progressive decrease of caliber.

Visualization of the coronary arteries was occasionally obtained during angiocardiography. Out of 1,200 cases, Gordon, Brahms, and Sussman observed one or both the coronary arteries in a dozen of them (the left, only in one case) They appeared with the above-described aspects

Retrograde aortography is a better method because of less dilution of the radiopaque substance and the absence of superimposed opaque shadows The direct visualization of an abnormal coronary artery reveals the existence of coronary lesions which is consistent with ischemic or myocardial lesions

Visualization of Ischemic or Necrotic Areas. The ischemic and necrotic areas do not present different opacity if they are within the cardiac mass, except in the case of calcification. Opaque *intramural thrombi* or opaque *arterial borders* are possible evidence of these lesions.

dial infarction. All of them are important in pointing to serious myocardial disease, especially when the clinical findings are equivocal.

In some instances, a striking reduction in amplitude of the ventricular deflections is the only effect of myocardial infarction upon the ECG. In some of these curves, the characteristic features of myocardial infarction may be recognized, but often they are not present. Commonly the form of the small deflections is bizarre or the QRS interval is prolonged because of intraventricular block. The complexes may be small throughout the ECG, but more commonly, the greatest reduction in size is seen in the standard leads, while there is little or no decrease in amplitude of the precordial deflections Curves of low voltage are not limited to myocardial infarction but are encountered at times in the presence of congestive cardiac failure, general anasarca, hydrothorax, pericardial effusion, and myxedema

Occasionally *intraventricular block* is caused by myocardial infarction. It varies from a slight increase in the QRS interval (Fig 10-12, curve of Oct 23, 1953, and Fig 10-14, curve of Oct 24, 1956) to complete BBB. The diagnostic characteristics of infarction may be obscured whatever the degree of block or the amplitude of the complexes, but they are usually preserved in right BBB (Figs. 10-13 and 10-16). In *left BBB* (Fig 10-14), the potential of the cavity of the left ventricle is positive initially, the initial negativity which is responsible for the characteristic Q waves is absent, and Q waves are not recorded, while the BBB deflections, because of their large size, dominate the curve and obscure the changes in the RS-T segment and in the T waves (Wilson et al., 1945). In rare instances, Q waves are present in leads over the left ventricle in left BBB and are attributed to additional *infarction of the septum*, which then transmits to the cavity of the left ventricle the initial negative potential of the cavity of the right ventricle. Similar considerations apply to leads over the right ventricle if it should be infarcted in the presence of right BBB.

Atrioventricular heart block, partial or complete, sometimes occurs after myocardial infarction, usually during the first few days and lasting only a few days. *Atrial fibrillation* sometimes occurs, while *atrial flutter* and *atrial paroxysmal tachycardia* are uncommon. *Premature beats* are common, usually of ventricular origin. *Ventricular paroxysmal tachycardia* is by no means rare and is a serious complication because it may exhaust the already weakened heart or lead to fatal ventricular fibrillation.

Rarely is the ECG normal in the presence of myocardial infarction, but occasionally the abnormalities displayed will be relatively

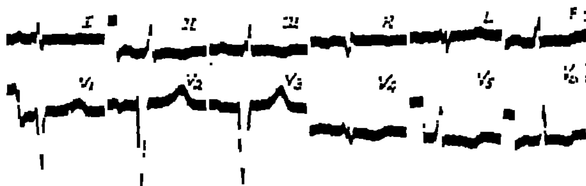


Fig. 10-17. Failure of the ECG to show evidence of myocardial infarction. Record of a 47-year-old man who had massive edema, ascites, enlargement of the liver, distended neck veins, clear lung fields, and premature beats and an extra heart sound in early diastole, but an otherwise negative examination. The venous pressure was elevated and the circulation time prolonged. There was no history of chest pain or dyspnea The ECG was reported as abnormal, showing rather small R waves in V_3, flat T waves in lead I, and inverted T waves in leads II and III and V_4, V_5, and V_6, but myocardial infarction was not considered. Autopsy showed old and recent infarction of the septum and anterior wall of the left ventricle and sclerotic occlusion of the anterior descending branch of the left coronary artery. Both clinical and electrocardiographic examinations failed to show evidence of myocardial infarction.

of the chest and the movements of the cardiac border.

The movable grid with slits of 1 mm placed at 30-mm intervals and moving vertically in 3 sec (motion of 10 mm/sec) gives the best information (Part 4, Chap. 8) The film may be examined vertically like any chest film. The author, however, suggested analyzing the waves of the border by placing the film in such a way that the curves are horizontal and the motion is from *left to right*, as in other physiologic records As inspiration decreases the height of the cardiac contractions, the roentgenkymograms should be recorded in apnea, even though there may not be a good visualization of the cardiac border (upper displacement of the diaphragm in obese individuals or in cases in failure) In every case, timing of the waves must be done by comparing the roentgen kymogram with tracings recording other evidence of cardiac activity which have been simultaneously recorded (ECG or aortic pulse registered on the same film)

The modifications of the left ventricular dynamics have been described as follows (Donzelot and Heim de Balsac)

Reduction in Amplitude The basic form of the ventricular waves (systolic retraction, diastolic expansion) of a certain point is preserved, but the amplitude is decreased to one-half or less of those recorded over other points of the ventricular border

Undulation and Reduction of Amplitude The systolic retraction and diastolic expansion are still visible, but the end and the beginning of systoles and diastoles are blurred

Tremulation Numerous small ripples substitute the normal waves so that it is difficult to distinguish systole from diastole.

Delay of Contraction. The waves do not coincide with those of other tracings recorded for reference and present a definite delay (an accurate chronologic comparison is always difficult because of weak exposure of the tracing).

Complete Immobility Certain segments of the cardiac border are completely immobile.

Paradoxic Movement. A segment of the border is nearly immobile, but there are small waves of expansion. Sometimes, the expansion is presystolic, while the end of systole has a plateau-like appearance or shows a delayed contraction which ends with a notch at the beginning of the diastole (partially reversed pulsation) A completely reversed pulsation of the ventricle (*retraction in diastole*, expansion in systole paradoxic pulsation) may occur Often the segments of altered dynamics are partly masked by localized or diffuse shadows due to adhesions, exudation, or stasis (Fig 10-19).

These alterations of left ventricular dynamics are the direct effect of the coronary lesions Tennant and Wiggers demonstrated this in experimental myocardial infarction in dogs The ischemic zone becomes immobile while the other parts of the ventricle still contract well This phenomenon is accentuated if there is shock and can be reversed by releasing the coronary clamp before tissue damage occurs. The diffuse or localized loss of myocardial contraction explains the decreased amplitude, the delay, and the systolic ballooning of the infarcted area under the thrust of intraventricular pressure

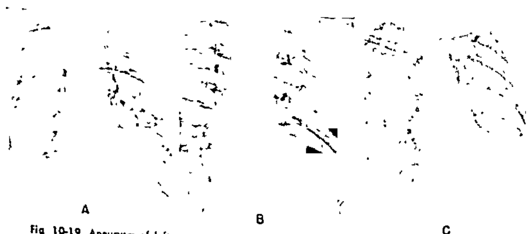


Fig 10-19 Aneurysm of left ventricle In (C) there is a rim of calcification of the upper part of aneurysm

Roentgenology and roentgen kymography in coronary heart disease

ROBERT HEIM DE BALSAC

In coronary heart diseases, the x-ray study supplies information in regard to the form and size of the heart and the large vessels The study of cardiac dynamics has in these diseases a particular interest Either angiocardiography or the existence of calcifications may reveal the location of an infarction. The observation of a parietal aneurysm of the heart is also an important possibility.

DIRECT EVIDENCE OF CORONARY HEART DISEASE

Coronary Calcifications. Calcification of the coronary arteries is often observed in anatomoradiologic examination of the heart postmortem (Pyke and Symons) (Fig. 10-18). Opaque spots or masses are noted along the course of the principal vessels, and especially at their branching. These calcifications are sometimes visible over long segments of the coronary arteries The infiltration of the arterial wall is shown by x-ray as continuous lines, giving the impression of long pipes In order to observe them in vivo, these infiltrations should be of considerable size (Lenk, 1927; Kuhlman, 1933, Snellen, 1937; Wosika and Sossman, 1939, Heim de Balsac and Marquis, 1941).



Fig. 10-18. Contrast visualization of coronary vessels.

The fluoroscopic observation of these shadows requires a prolonged accommodation of the eye, deep radiation (90 kv), high intensity (5 ma), and a very luminous screen. To register them on a film requires a short distance (0 60 m), 115 kv and 180 ma, with grid and use of a spot film. The duration of exposure is a function of the power of the apparatus. It is necessary to close the shutters as much as possible in order to reduce the field to a rectangle of a few square centimeters and to include only a part of the cardiac shadow, in order to avoid the blinding contrast with the clear adjoining areas

The best area of visualization of the coronary arteries is within the left middle arch, corresponding to the course and branching of the left coronary artery, which are frequently altered Very seldom are coronary arteries visualized in other areas of the cardiac shadow. The coronary arteries are observed as interrupted lines, tortuous or branching, comparable to strands of straw Only in one case was

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Electrokymography and other graphic tracings in coronary heart disease

ALDO A. LUISADA AND ALDO JACONO

PHONOCARDIOGRAM

The most typical change observed after a myocardial infarct is the disappearance of the rapid vibrations of the 1st sound. This sound then presents a prolonged series of slow vibrations which are frequently small but may be of normal height. After the acute stage, it is possible to observe large extra sounds in diastole (*triple rhythm, quadruple rhythm*). These additional sounds are heard only if they are very loud, on account of their low pitch (Fig. 10-20 and 10-23B).

LOW-FREQUENCY TRACINGS OF THE PRECORDIUM

Cardiographic tracings are obtained with difficulty in the acute stage of myocardial infarction because of weak cardiac action. When a good tracing is obtained, a slow development of all waves is usually observed (Fig. 10-20). This is due to the existence of an area of soft tissue in the left ventricle. By absorbing part of the energy of contraction, this area prevents a rapid rise of pressure and may even cause a less rapid closure of the mitral valve. Therefore, while the 1st sound becomes al

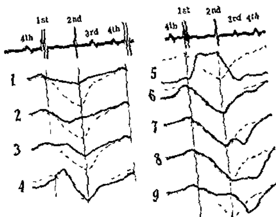


Fig. 10-21. Scheme of the abnormalities of the ventricular EKy (continuous line) compared with the normal tracing (dotted line). 1. Decreased amplitude of contraction. 2. Early end of contraction. 3. [illegible] onset of contraction. 4. Early systolic distention [illegible] distention. 9. Decreased amplitude of contraction and deep early diastolic drop (From Luisada and Fleischner. Acta. Cardiol. 1948.)

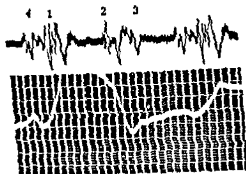


Fig. 10-20. Phonocardiogram (stethoscopic) and low-frequency tracing at apex in a case of coronary heart disease and history of an infarct. Quadruple rhythm. Slow diastolic waves. Slow motion of apex.

In conclusion, the direct radiologic evidence of coronary disease is, so far, more a clinical curiosity than an important part of the current study.

INDIRECT EVIDENCE OF CORONARY DISEASE

Coronary artery lesions and ischemia or necrosis of the myocardium may occur without modifications of the volume of the cardiac chambers or of the large vessels. The heart often appears normal in shape, size, and position, while the aorta may show alterations of the wall due to senility. In other cases, on the contrary, the lesions of the coronary arteries are widespread or are associated with other diseases, such as hypertension. Previous coronary attacks may have left their mark, and there may be evidence of hypertrophy, myocarditis, or diffuse myocardial damage. In these cases, the heart and vessels show roentgenologic changes The typical aspects of cardiac enlargement (predominantly left) consist of convexity of the left border and apex, sinking of the apex into the diaphragmatic shadow, persistence of the left ventricular prominence in the LAO position, and its bulging in the RAO or in the lateral positions. Evidence of vascular damage is revealed, on the other hand, by broader aortic shadow, bulging of the ascending aorta on the right, visibility of the descending aorta on the left, a characteristic curvature of the arch in the LAO position, its "swan-neck" shape in the RAO position, and possibly *aortic calcification*

In addition, in cases with failure, it is possible to observe the signs of *pulmonary congestion* haziness of the hila, congestion of the bases, and *pleural effusions*, either localized in the scissures or diffuse These signs are not characteristics of coronary heart disease and do not add any definite information which can be of use for an etiologic diagnosis More important are the modifications of the cardiovascular organs which can be observed in comparative studies over months or years. Particularly, after an episode of myocardial infarction, the size of the cardiac shadow may either be unchanged or increase as a result of heart failure connected with a more or less wide destruction of left ventricular muscle

The author has studied the large vessels of the base in patients with coronary heart disease and seldom found definite changes. On the other hand, these patients often present *dilatation of the branches of the pulmonary artery*. It is possible to observe evidence of *adhesions* which form over the ischemic or necrotic areas. These pericardial and pleuropericardial adhesions are revealed by opaque images along the cardiac border, or as strands crossing the shadow of the cardiac mass and spreading in the pulmonary fields, or in case of old lesions, as the shadow of a scissuritis connected by a small triangle to the cardiac border.

Laubry, Soulié, and Heim de Balsac described the fixation and elevation of the left diaphragmatic dome, simulating the results of a phrenicectomy. This may be due to the irritation, compression, and paralysis of the phrenic nerve because of inflammation or adhesion in its course along the pericardium.

In conclusion, some of these data give indirect evidence which may confirm the existence of coronary heart disease. The others reflect independent changes of the vessels and heart during coronary disease.

FLUOROSCOPY, ROENTGEN KYMOGRAPHY. CARDIOVASCULAR DYNAMICS

The study of cardiovascular dynamics, generally neglected, is of great diagnostic importance in coronary heart disease. Numerous authors (Shilling; Master; Gubner, Levene) have studied cardiac dynamics by fluoroscopy after myocardial infarction and have observed anomalies of contraction of the cardiac border over different points. The characteristic modifications observed by them were reduction of the pulsations, complete immobility, or paradoxic expansion (immobility or incomplete contraction of the apex). These subjective observations may give useful information to the cardiologist, but a more exact study requires an objective method of recording (Dack, Gubner, Levene; Master; Perona; Stumpf; Heim de Balsac; Cignolini). The author considers roentgen kymography as an essential and routine method of study in coronary heart disease Electrokymography, which is even more instructive, will be described below.

The author uses *teleroentgen kymography* (distance from the anticathode to the film, 2 m), which gives in the same film the picture

either the apex or the lateral wall; in 1 case (incompletely studied), a posterolateral abnormality was found, in 1, no abnormality. In 7 cases, there was a history of repeated episodes of infarction or of attacks of severe, prolonged precordial pain. In all of them, marked abnormalities of contraction were found in the anterior, posterior, and lateral walls The only remaining case had an ECG indicating left ventricular strain, while a large area of the lateral wall of the left ventricle presented abnormalities of contraction These coincidences amount to nearly a 90 per cent identity in the topography of the lesion between the ECG and EKy

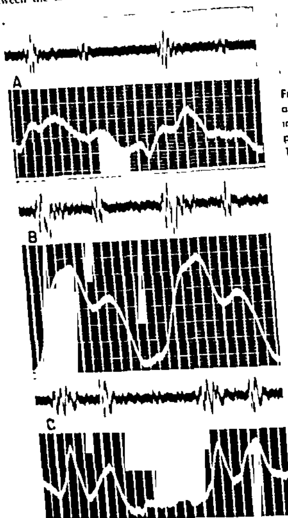


Fig. 10-24 Abnormal pulsations of lateral border in case of posterolateral infarct A EKy of apex. minimal systolic distention B. EKy above apex severe systolic distention (paradoxical pulsation). C. EKy at upper left borders double pulsation.

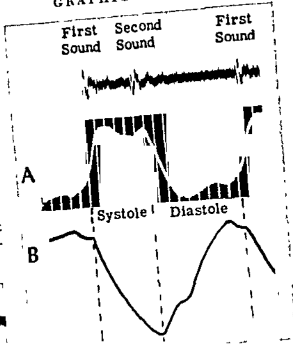


Fig. 10-25 Old anterolateral infarct with dynamic aneurysm. A Paradoxical, plateau-like expansion in systole B Scheme of normal pulsation, for comparison (From Luisada Med. Clin No. America 1952)

Some of the abnormalities can be found in other conditions than myocardial infarction. For example, a marked *diastolic rebound* was found in acquired valvular lesions and in ventricular septal defects, initial distention followed by contraction was found in certain cases with aortic insufficiency or arterial hypertension Presystolic distention may be found in cases with an atrial type of triple rhythm Therefore, these abnormalities have *no* diagnostic significance in regard to myocardial infarction Some of the diastolic abnormalities are related directly to abnormalities of systole and represent a necessary consequence of the latter Whenever an inverted movement in early diastole follows an inverted systolic pulsation, it is apparent that it is connected with it and does not deserve special mention On the other hand, an inverted diastolic wave can be found as an isolated phenomenon, and then it represents a well-defined and noteworthy abnormality

A *rebound in early diastole* represents a typical abnormality whenever it is marked and constitutes a seemingly new wave in that phase. The opposite phenomenon is repre-

In human beings, the conditions of examination after a myocardial infarction are unfavorable. However, Sampson and Dack described the rapid appearance of dynamic alterations. At the beginning, as a rule, there is a paradoxic expansion, later, during the evolution of the lesions, one or the other of the previous types of changes is observed. Therefore, the functional disorders revealed by roentgen kymography are logically connected with the sequence of structural changes.

The different modifications of left ventricular dynamics represent a wide range, from the simplest (reduction of amplitude) to the more severe (paradoxic systolic expansion). These alterations are usually observed at the apex, but they spread more or less toward the base according to the severity of the case. When two or more types of dynamic changes are observed, the *most severe are always at the apex*. In certain cases, the entire left ventricular border is immobile, corresponding to widespread and severe myocardial damage. The oblique positions show the horizontal extension of the dynamic alterations They are more evident in the RAO position and decrease progressively in severity when the rotation is changed to the LAO position

In patients with coronary disease, alterations of left ventricular dynamics are observed with great frequency: the author recorded them in 91 per cent of cases (141 times in 155 subjects examined) They are localized in 125 cases (80 per cent) and extended to the entire left ventricular border in 16 cases (10 per cent).

The frequency of the various types of changes is as follows. undulation and reduction, 48 per cent, tremulation, 50 per cent; complete immobility, 56 per cent, paracardiac blurring, 50 per cent, delayed contraction and paradoxic pulsation, more rarely These values are in accord with the findings of Master, Dack, Susmann, and Prinzmetal They are found both in anterior and posterior myocardial infarction The ischemic or infarcted areas localized by electrocardiography do not correspond exactly to the localization of anomalies of left ventricular dynamics because the latter are most often at the apex. This was confirmed by Heim de Balsac and Alessandris in a series of 71 cases of posterior infarction Increased severity of disorders is revealed by the fact that a complete immobility substitutes undulation or reduction of pulsations, on the other hand, even in case of improvement, the paradoxic pulsation is usually irreversible.

The evolution of left ventricular dynamic changes is not strictly connected with that of the electric changes. The amplitude of the contractions may decrease before any other clinical signs; it may follow an evolution parallel to that of ECG changes; or it may evolve in a complete opposite manner: normal dynamics is then found with still abnormal ECG or, on the contrary, persistence of an altered dynamics when the ECG has returned to normal. In the same way, the alterations of ventricular dynamics in patients with coronary disease are not directly related to other signs of altered myocardial function, such as triple rhythm (gallop rhythm) or dilatation of the heart. The roentgen kymographic study of cardiac dynamics supplies important data in coronary diseases, which help, not only for diagnosis, but in order to follow the evolution of the disease. Therefore, the author considers left ventricular roentgen kymography as a routine test to be done in all patients with coronary disease. The variations observed are neither surprising or illogical: cardiac dynamics, vibrations revealed by auscultation, changes of intracardiac pressures, and changes of the electric forces are different phenomena, all related to the ventricular activity but not necessarily connected Therefore, their modifications may be discordants.

The study of cardiac dynamics opens the way to new concepts. The observation of larger contractions over the posterior contour of the left ventricle leads to the belief that the left ventricular contraction is not concentric, but has a greater amplitude in a PA plane than in a lateral. The fact that the left ventricle continues to propel blood when all its left border is immobile leads to the belief that, in such cases, the posteroinferior wall and the septum perform all the necessary work The frequency of the dynamic changes observed at the apex, even in cases of posterior infarction, is more difficult to explain. Master and Dack suggested that it is due to the spiral arrangement of the myocardial bundles inserted on the valvular rings.

2. *Inverted pulsation (paradoxical pulsation) of a circumscribed area of the ventricular myocardium.* In typical cases, this inverted pulsation assumes the aspect of a *plateau*, indicating that the inert wall is passively distended by intraventricular pressure. This type of pulsation may be associated with the existence of a well-defined bulge of the ventricular silhouette on chest films. In such cases, the name of *ventricular aneurysm* should be used. In other cases, bulging occurs only in systole while no bulge is present in diastole. This phenomenon, occasionally observed on fluoroscopy, is hardly noticeable on roentgenograms, these, even if taken at the maximum of systole, would show but a minute projection, hardly detectable without simultaneous observation of the two opposite motions

It should be kept in mind that the dynamic significance of such an inverted pulsation is similar to that of an aneurysm The wall distends in systole, absorbing part of the dynamic effort of the normal myocardium, it collapses in diastole, disturbing the normal filling and spilling its retained blood into the rest of the ventricular cavity This similarity, already emphasized by Murray (1947), justifies the term of "dynamic aneurysm" in instances where a typical inverted pulsation is found without any persisting bulge in the profile of the left ventricle It is likely, though not yet demonstrated, that a dynamic aneurysm corresponds to the formation of a "niche" in the ventricular wall, i e, to a remarkable thinning of the wall This fact, which pathologists still call "aneurysm," may not correspond to an aneurysm in a chest film Thus, the EKy is more accurate in its recognition of a severe lesion of the wall than the chest film

Both these typical phenomena, the lack of pulsation and the inverted (or paradoxical) pulsation, were encountered either on the anterior or posterior wall, respectively, or in one of these locations but also extending to the lateral wall, or in a large area including anterior, lateral, and posterior walls The most common occurrence is that of either an anterior or a posterior location with extension to the lateral wall

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The above observations reveal functional pulsatory disturbances, and not necessarily irreparable anatomic damage. Repeated observations over a long period of time may reveal return to normal pulsatory function in some instances, while in others, local paralysis or paradoxic pulsations will be persistently observed, indicating irreversible structural damage, probably fibrosis.

The areas of myocardium surrounding the site of occasional damage, as revealed by absent or inverted pulsation, frequently exhibit minor abnormalities They may be due to either functional disturbances at the periphery of the lesion or mechanical repercussion. It is apparent that irregular traction and shaking may occur in the border-line zone between severely damaged and normally functioning myocardium

In general, the findings of electrokymography confirm those of roentgen kymography. However, the electrokymographic method, because of the distinctness and wealth of detail as to timing and configuration of the recorded waves, and the easy approach to the anterior and posterior walls of the left ventricle, permits a better and more accurate evaluation of the various abnormalities.

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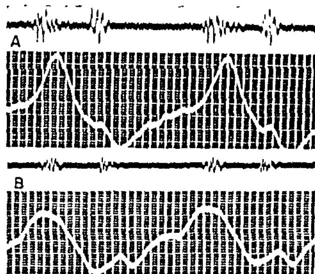


Fig. 10-22. Electrokymogram in a case of anterolateral infarct. A. Early systolic distention followed by normal contraction at apex. B. Normal dynamics above apex.

tered, all the low-frequency vibrations of the chest also become slow (Fig 10-20).

ELECTROKYMOGRAM

Electrokymography permits an accurate study of the movements of the left ventricular walls and gives tracings which may have diagnostic value.

Various abnormalities have been observed (Luisada and Fleischner; Dack et al, 1950, Samet et al) (Fig 10-21) Some of them have been found typical of a circumscribed damage to the ventricular wall; others, on the other hand, are not specific and may also be observed in cases with diffuse myocardial damage.

Several abnormal patterns were observed *during systole* Four of them can be grouped together, being an expression of the same phenomenon, i e, a decreased amplitude of the ventricular wave of contraction (Fig. 10-22): reduced amplitude, early end, late onset, or absence of the wave

Two other systolic patterns reveal a more advanced disturbance because they indicate a tendency toward distention (Fig 10-23 to 10-26)· (1) *early distention* followed by a normal ventricular wave, (2) *inverted pulsation* (so-called *paradoxical pulsation*).

In addition to these, a bizarre phenomenon consisting of an M-shaped complex during systole was occasionally observed Various abnormal patterns can also be observed during diastole: (1) marked rebound in early diastole (systolic-diastolic M) (Fig. 10-21); (2) absence of rapid rise in early diastole, (3) drop of the tracing in early diastole, (4) marked distention during presystole

CORRELATION OF ELECTROCARDIOGRAPHIC AND ELECTROKYMOGRAPHIC FINDINGS

Out of 20 cases studied by the authors, 7 were instances of relatively recent myocardial infarction (patients studied within 3 to 6 weeks from the onset of the attack), 8 were instances of old infarctions which had taken place from one to several years previously. The other 5 cases had had repeated infarctions but were also observed within 3 to 6 weeks after a new episode. In 4 cases, the ECG indicated *posterior myocardial infarction;* in all of them, the abnormality of contraction was located in the posterior wall and extended to the lateral wall.

In 8 cases, the ECG indicated *anterior or anterolateral myocardial infarction.* In 6 of them, the abnormality of contraction was located in the anterior wall and extended to

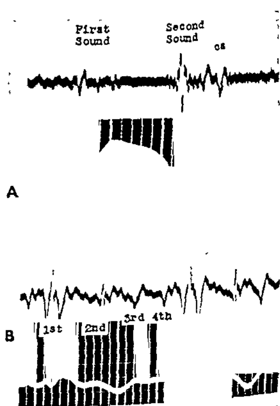


Fig. 10-23. Electrokymogram in a case of anterolateral infarct. A. "Paradoxical pulsation" (or plateau-like distention) in systole at apex. B. No contraction above apex.

8

Cardiopexy

SAMUEL A. THOMPSON

Value of Surgery. In myocardial ischemias, and especially in coronary disease, some patients sustain severe myocardial damage and are incapacitated beyond the stage of satisfactory recovery Surgery may offer these patients a chance for further rehabilitation which cannot be secured by nonsurgical methods During the course of coronary disease, a change from ischemia to hyperemia of the myocardium can give some protection from further serious damage by the ischemic process Thus the value of surgery in coronary disease is chiefly that of rehabilitation and protection.

Principles of Surgery. There are two general principles in the surgical treatment of coronary disease One is *palliative* and consists in interrupting the nerve pathways through which the painful impulses are carried The other is *definitive* and consists in the development of an additional blood flow and distribution to the myocardium, known as revascularization

METHODS OF REVASCULARIZATION

Two equally important factors must be considered in correcting myocardial ischemia they are an increased volume of blood and a satisfactory distribution of this blood through the myocardium Failure to establish either of these will result in failure to correct the ischemia

The gradual narrowing and final occlusion in coronary artery disease occurs principally in the main arteries rather than in the secondary branches, and either the right or left side may be primarily involved Correcting an insufficient myocardial blood supply and distribution should be aimed at the entire myocardium and not at the right or left ventricle Much of the present-day surgery for the relief of coronary disease is directed toward increasing the blood volume delivered to only one section of the myocardium, namely, the left ventricle, and yet the right ventricle may be the site of the greatest pathologic changes.

Overcoming an inadequate blood distribution because of a blocked coronary system must be done through the growth of new blood vessels or new anastomoses between already existing vessels, such as the communication of extracardiac vesels with the coronary system, distal to the obstruction, and stimulating an increase in the inter- and intracoronary anastomoses.

Sources of Collateral Supply. The source of the additional blood flow may be extracardiac, intracardiac, or a combination of both. The *extracardiac source* may be from vascular or tissue grafts or from the development of the *residual myocardial circulation* The term residual myocardial circulation indicates those small blood vessels which actually constitute a preformed source of collateral circulation (Hudson et al). They have their origin around the base of the heart and great vessels and from the pericardium When the coronaries become blocked, they are the principal remaining sources of blood supply This circulation is capable of tremendous growth and expansion under proper stimulation, and one of the strongest stimulants is local or surface irritation of the pericardium and myocardium

A method of increasing the residual myocardial circulation through the pericardium is the *bilateral ligation of the internal mammary*

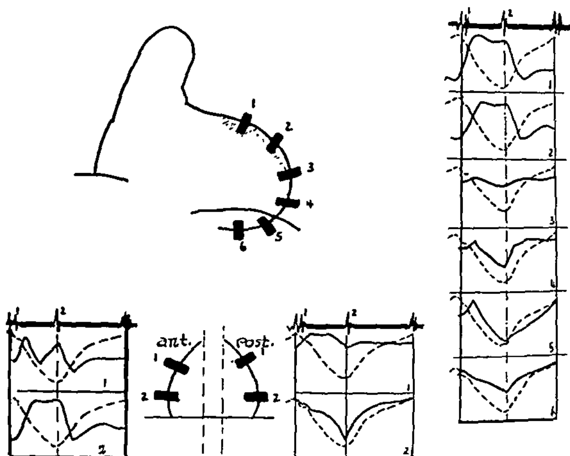


Fig. 10-26. Location of the slit and reconstruction of dynamic changes in a case with multiple infarctions. Large dynamic aneurysm extending from the upper part of the lateral wall to the lower part of the anterior wall. Absence of contraction in the mid-lateral and posterior walls. (*From Luisada and Fleischner Acta Card.* 1948.)

sented by the *lack of a diastolic return of the tracing toward the base line* This may or may not be connected with abnormalities of the systolic wave. When isolated, this phenomenon is worthy of note and is significant It should be kept in mind, moreover, that some of these deviations from the normal tracing, and particularly those extending over a large portion of the left ventricular contour, are apt to be due to *positional changes* of the heart.

Two abnormalities of ventricular systole, the *late onset* and the *early end of the ventricular wave*, were encountered in cases of infarction but in no other cases, so far. Nevertheless, they should not be considered as having a diagnostic value unless positional changes can be ruled out.

Two abnormalities of the systolic wave have been considered diagnostic of localized myocardial damage, in the majority of instances this being identical with myocardial infarction: [1]

1. *Reduced amplitude of the ventricular wave or disappearance of this wave in a circumscribed region of the left ventricle.*[2] Whenever the surrounding areas present large waves, this sign is definitely related to infarction As that area is functionally (and usually also anatomically) excluded from participating in active contraction, the authors have suggested the name of *local paralysis* for the phenomenon thus revealed by electrokymography

[1] This rule, while undoubtedly true in the great majority of cases, may have its exceptions Myocarditis usually causes *diffuse changes* However, the authors have observed two cases of rheumatic heart disease with valvular lesions in which a localized "paradoxical" pulsation was recorded. In one of them, subsequent autopsy revealed a large patch of fibrosis in the anterolateral wall of the left ventricle caused by old, healed rheumatic myocarditis.

[2] Landowne has remarked that the pattern of "local paralysis" indicates that the damaged area fails to move inward like the rest of the ventricular wall. Thus, it is equivalent to a moderate relative expansion. If this explanation is accepted, "local paralysis" would be equivalent to an initial "dynamic aneurysm."

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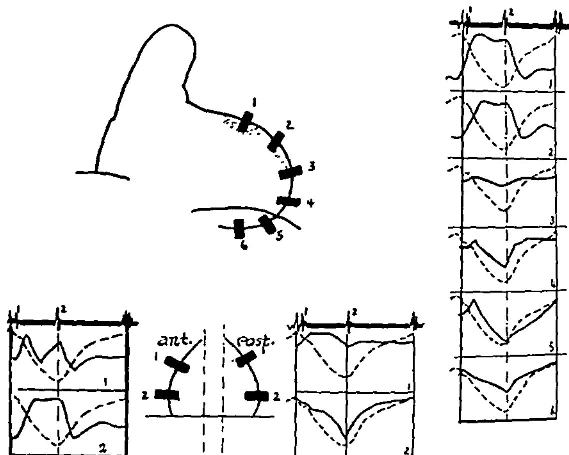


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the application of asbestos fibers scattered over the raw areas. The partial occlusion of the coronary sinus is done by an encircling ligature tied down over a 3-mm probe Beck and Brofman (1956) report very satisfactory results with this method.

BENEFITS

The benefits from cardiopexy are rehabilitation, protection, and increase in life span. Rehabilitation comes through relief of pain and improvement in the exercise tolerance. There is protection from fear of the agonizing precordial pain coming on at unpredictable times of the day or night. There is also some protection from the fear of possible sudden death, as less than 1 per cent of cardiopexy patients (who survived the operation for as long as 3 months) have died suddenly The percentage of sudden deaths in the unoperated cases of coronary disease is much higher A study of the patients who have died subsequent to a cardiopexy and a comparison with groups of unoperated patients with coronary disease who have died leads us to believe that the life span of the operated patients averaged more than 5½ years longer than the unoperated patients

TESTS OF REVASCULARIZATION

Evidence of revascularization can be seen by the following five tests

TESTS FOR MYOCARDIAL REVASCULARIZATION

1 *Intercoronary–peripheral coronary backflow* following a central occlusion
2 Extracardiac–retrograde aortic filling of coronary arteries
3 Continued myocardial contraction in the zone of an occluded coronary artery
4 Failure of myocardial contraction when the collateral flow is removed
5 Tests of clinical improvement

The peripheral coronary backflow represents the basal intercoronary anastomosis Retrograde aortic filling of the coronaries by this maneuver is definite evidence of extracardiac anastomosis Myocardial contractions cease when the blood flow is cut off The clinical tests include relief of precordial pain, increase in exercise tolerance, performance of daily duties, and a return to some gainful occupation

The first is a test of *intracardiac collateral blood flow* as measured by the peripheral coronary backflow in both quantity and oxygen content following a central occlusion In the normal animal, the volume is about 1.7 ml/min Following cardiopexy, this volume is increased to 5 3 ml/min Bakst).

The second test is for *extracardiac collaterals* and is done by placing a clamp over the ascending aorta just above the origin of the coronaries, a second clamp is placed just above the diaphragm. This isolated section of aorta is then injected with a colored opaque solution of plastic material. In the normal animal, the coronaries are not filled by this maneuver. Following cardiopexy, this test shows filling of the coronaries in 50 per cent of the animals and is definite evidence of extracardiac anastomoses (Bakst).

The third test is *continuation of myocardial contractions in the zone supplied by an occluded coronary artery*. In normal animals, following complete occlusion of the anterior descending coronary artery, there was about a 50 per cent mortality from ventricular fibrillation or infarction. When the same occlusion *is done 2 weeks after cardiopexy*, the mortality is zero (Gregg and Dewald).

Failure of myocardial contraction when the source of the collateral flow is removed is the fourth test. In a group of animals who had a preliminary cardiopexy, a series of operations was performed in which both coronaries were ligated up to their origins Then, as a last procedure, the adherent pericardium, through which the collateral flow came, was removed, and none of the animals survived.

Clinical improvement of the patient is the fifth test While this test may be considered subjective by some, it is certainly the most important in so far as the patients are concerned This is measured by the relief in pain, the improvement in physical exercise tolerance, the ability to perform daily duties, and the return to a gainful occupation.

These five tests appear to give conclusive evidence of myocardial revascularization Any patient with coronary disease, with or without *a previous infarction*, who remains physically incapacitated as much as 50 per cent because of pain or dyspnea, should be considered as a candidate for surgery. The two principal contraindications are an acute or unhealed infarction and intractable congestive failure.

RESULTS

Cardiopexy was devised and first performed by the author in 1938, and that first patient is still living Since that time, the author has operated upon and observed over 400 patients. The following data shows the results: there is an operative and hospital *mortality* of approximately 5 per cent Using the clinical tests described above, 10 per cent of the patients have

raphy demonstrated clearly the results of both the recent and old lesions (Gubner and Crawford, 1939; Dack et al., 1940). The authors had the same experience with electrokymography. They had the general impression that the myocardial lesions, revealed by the EKy, were more extensive than those indicated by electrocardiography, since the lateral wall appeared to be involved frequently even in cases of frank "anterior" or "posterior" infarction

While a "dynamic aneurysm" is typical of the scarring of an old infarct, experimental studies (Tennant and Wiggers) and roentgen kymographic observations (Dack et al) indicate the likelihood that a recent infarct also presents this phenomenon.

9

Surgery of coronary heart disease

ARTHUR M. VINEBERG

The treatment of coronary heart disease by medical or surgical means has been and still is most difficult—as well as unsatisfactory. This is attested to by the ever-increasing mortality and morbidity of the disease, which is now responsible for at least one in four deaths that occur in North America

As the disease is said to be unpredictable in its course, any form of treatment is difficult to evaluate. It has, in fact, been stated that "almost anything may cure precordial pain" This statement would be correct if it were modified to read, "almost anything may bring about temporary relief from precordial pain"

Credit for beneficial treatment, whether medical or surgical, has frequently been based upon sketchy pre- and postoperative evaluation of a patient's disease There are many reasons for this situation, mostly based upon misunderstanding, disagreement, and confused thinking. In this chapter, some of the thinking about the treatment of coronary heart disease will be reviewed so that, wherever possible, generally accepted facts may be listed, and the role of surgery in the treatment of coronary heart disease examined in their light

CORONARY CIRCULATION IN HEALTH AND DISEASE

The coronary circulation is different from that of any other circulating system in the human body It is necessary for all students of coronary heart disease to understand something about the complexity of the structure and function of the heart of man and lower animals In the past, there have been many disagreements concerning the character of the coronary circulation, particularly in reference to the anatomic vascular channels that lie within the ventricular myocardium and to their connections between the coronary and mediastinal vessels. During the past few years, a clearer picture has emerged, so that now there are certain facts about which there appears to be general agreement.

Two large arteries leave the aorta just above the right and left aortic cusps to form the main right and left coronary arteries, respectively.[1] The left coronary artery divides into the anterior descending septal and circumflex coronary branches. These large coronary arteries lie on the surface of the heart beneath the epicardium. Each large artery supplies a separate zone of arterioles lying within the myocardium Under normal conditions, there is little or no connection between the myocardial arteriolar zones supplied by the four major coronary arteries, it is for this reason that for many years the coronary arteries were considered to be end arteries [Fig 10-26(1)]. This view was tenable until Schlesinger and Zoll, through radiopaque injection studies of human coronary arteries, demonstrated the presence of numerous arteriolar-size branches running between different coronary arteriolar zones They found these communications to exist when there was narrowing or occlusion of coronary arteries in their epicardial courses. These types of communication between arteriolar zones or between arteries have been termed "collaterals" and have been shown to exist in 9 per cent of normal human hearts and in practically all human hearts with evidence of myocardial ischemia caused by coronary artery narrowing.

The "Collateral," Its Development and Distribution. For years physicians have been saying that if a patient is given time, he will develop his own collaterals and thus heal himself, further, that

[1] See Part 1, Chap. 6. *Editor.*

arteries just below the pericardiophrenic branches (Battezzati et al.). This produces an increased vascularization of the pericardium. The full benefit of this increased vascularization cannot be utilized unless there is an intimate connection of the pericardium to the myocardium with communication of the pericardial and myocardial vessels below and distal to the coronary obstruction.

USE OF GRAFTS

Many tissues have been used as grafts, but the one tissue which has been most successfully used for a long period of time is the pericardium (Thompson, 1940). The blood supply of the pericardium is abundant and is especially suited because of its proximity. The formation of a granulomatous graft or an area of granulomatous tissue between the graft and host is a valuable addition, provided that this granulomatous area is permanent. In addition to being composed principally of blood vessels, the granulomatous area acts as a bridge through which the extracardiac and intracardiac blood vessels can communicate and through which the vascular continuity can be reestablished proximal and distal to an occlusion.

At the present time the principal vascular graft used is the *internal mammary artery* This operation was devised by *Vineberg*, who has used it successfully for a number of years.[1] However, the greatest increase in the intracardiac blood flow comes through the development of intercoronary and intracoronary anastomoses, giving a more extensive and adequate distribution of the blood This is best accomplished by *surface or local irritation of the myocardium* The importance of irritation is great for irritation produces inflammation and inflammation results in *hyperemia*, which is the reverse of myocardial ischemia Prolonged irritation is better than temporary, and if the irritation is permanent, the best results may be expected.

Another method of myocardial revascularization which utilizes both increased blood supply and distribution is *cardiopericardiopexy* (cardiopexy, for short) This is essentially a form of *permanent surface irritation* and is accomplished by distributing an irritant powder over the surface of the epicardium. This irritant powder (magnesium silicate–U.S.P. talc) is not absorbed by the lymphatics or removed by the phagocytes and results in an area of granulomatous tissue, adherent on its outer side to the pericardium and on its inner side to the myocardium. This granulomatous adhesive area acts as a vascular bridge for the communication of blood vessels of the pericardium and mediastinal structures with those of the coronary system. The irritant also improves the intracardiac blood distribution by stimulating an increase in the number of new vessels to the myocardium beyond the site of the occlusion, as well as an increase in the intercoronary and intracoronary anastomoses. The granulomatous area never changes to scar tissue nor becomes avascular, because the irritant is never removed and it thus acts as a permanent source of collateral circulation The author has been able to demonstrate the permanency of the blood vessels in the granulomatous area as well as the continued presence of the irritant powder crystals by autopsy on patients who have died as long as 10 years after cardiopexy. The technique of cardiopexy has been described in detail (Thompson et al, 1954) and the following is a summary.

The approach to the heart is over the fifth left costal cartilage, which is removed. This approach is used because the pericardium is exposed without entering the pleural cavity. After a small opening is made in the pericardium, all fluid is aspirated to prevent the powdered talc from being washed to the dependent recesses of the pericardium The irritant powder is then widely distributed over the anterior surface and borders of the myocardium No attempt is made to cover the posterior surface as some of the powder is carried there by the beating action of the heart The pericardial opening is loosely closed, and the chest wall structures are closed in anatomic layers without drainage.

This procedure is simple, has a low mortality, and can be used in severely handicapped patients. The addition of bilateral ligation of the internal mammary arteries may further increase the good results of cardiopexy.

Another method of myocardial revascularization *is* the one used by Beck since 1950 This is *a combination of surface irritation plus a partial occlusion of the coronary sinus* The surface irritation is produced by mechanically scarifying the lining epicardium of the pericardium and myocardium. This is followed by

[1] See Chap. 9. *Editor.*

arteriolar collaterals have developed to aid a more even distribution of blood throughout the heart muscle.

The problem thus resolves itself into a mechanical hydraulic one Coronary arteries *supplying blood to an area of the myocardium* have a well-established cross section which permits a maximum quantity of blood to flow through their channels into that area. It has been said that occlusion *of one major coronary artery* is necessary *to produce precordial pain.* It is evident that if one major coronary artery is occluded and another artery is somewhat narrowed, the third coronary artery cannot supply *the* amount of blood formerly *supplied* by the blocked and narrowed vessels This situation, therefore, results in either progressive slow death of the myocardium or sudden death in the form of myocardial infarction

The point of critical *coronary* artery narrowing has been clearly substantiated in the experimental laboratory at McGill University. It has been shown in animals that when two major coronary arteries, the anterior descending and circumflex arteries, are narrowed by amerond constrictors to 50 per cent or more of their average lumens, the animals will die within a 28-day period In roughly 15 per cent of the animals, there is a large connection between the right and left *coronary arteries. In* such instances, the animals may survive partial constriction of their two major left coronary arteries. It is thus clear that ischemia in the human or animal heart stimulates *only the collaterals that lie* between the arteriolar *zones* and b*etween* coronary arteries. There is no evidence *to indicate that in the diseased* human heart, *or in* the animal heart artificially made ischemic, there is an ingress of extracardiac arteriolar-sized blood channels into the myocardium.

The Myocardium as a Vascular Sponge. The vascular structure *of the myocardium* has been the subject of much controversy over the past 75 years Debate has centered on the existence or absence of (1) vessels in the heart walls communicat*ing* with the heart chambers; (2) vascular spaces lying between myocardial fibers, other than the capillary system.

Wearn, in a brilliant piece of work, clearly defined the relationship of thebesian arteriolumınal vessels and *myocardial sinusoidal* spaces. His conception of the vascular structure of *the myocardium* has been confirmed by others, including the author [Fig 10-26(4)] The concept of Wearn and the author concerning the structure of the coronary circulation, *if correct, permits of the theory* that the myocardium may obtain oxygenated blood from two sources, viz., (1) the coronary arterial tree, (2) the lumen of the ventricle. It is theo*retically possible for the* blood to be siphoned back into the ventricular wall *through arteriolu*minal and myocardial sinusoidal spaces during diastole, when such spaces are empty. This can happen *only in the diseased heart,* where there is little or no forward flow *into the myocardium* through the narrowed coronary arteries *During systole, the* vascular spaces of the myocardium are emptied by the squeezing action of the myocardial fibers and the blood is moved into the venous system [Fig 10-26(5)].

Myocardial sinusoidal spaces have *been frequently* shown in the author's laboratory. Because

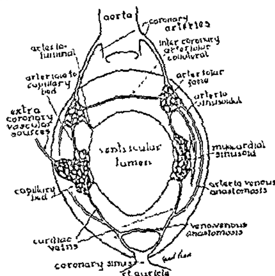


Fig. 10-26(4). Myocardial circulation.

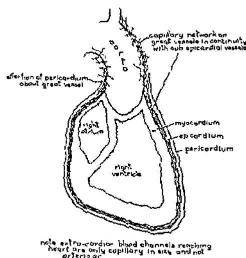


Fig. 10-26(3). Type and course of mediastinal vessels entering heart.

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[1] See Chap. 9 *Editor.*

THE HEART The effect of coronary artery disease upon the heart is related to many factors, a great number of which are still unknown, and others unexplained The myocardial fiber, which fundamentally is the unit of life, requires oxygenated blood in varying amounts When a segment of myocardial fiber suffers diminution of blood supply because of narrowing of the supplying coronary artery, the area becomes anoxic This may go unnoticed by the patient and, if it progresses, may result in the death of the affected area, forming a silent myocardial infarction In most cases, however, the patient receives a warning of the area of myocardial ischemia and experiences precordial pain

It is safe to say that precordial pain is generally accepted as a symptomatic reflection of myocardial ischemia caused by coronary artery insufficiency, and that when it occurs at least one major coronary artery is severely narrowed When precordial pain persists in spite of medical therapy, there is no agreement as to the extent of myocardial fiber damage that may result In the author's opinion, persistent precordial pain reflects continuous myocardial ischemia which results in progressive destruction of myocardial fibers

Hill has shown that the longer the history of precordial pain is, the poorer the operative risk is and the less likelihood there is of a good result after revascularization

Progressive destruction of myocardial fibers, whether due to chronic ischemia or to repeated acute myocardial infarction, usually leads to left ventricular failure It may result in ventricular aneurysm, ruptured papillary muscle, or interventricular septal defect

VENTRICULAR FIBRILLATION Another possible result of severe hypoxia or anoxia of the myocardial fiber is ventricular fibrillation It has been shown by Beck that a small area of anoxia in the ventricular myocardium is sufficient to send the heart into ventricular fibrillation, with resultant death, unless the heart can be immediately defibrillated. Beck has frequently stated that these hearts "are too good to die" Immediate defibrillation has resulted in the resuscitation of a great number of patients who are living normal lives several years later

Excluding the question of endocardial nutrition, the facts just mentioned have been proved by many and are now generally accepted

SURGICAL PROCEDURES FOR THE TREATMENT OF CORONARY ARTERY DISEASE

Operative procedures are designed to (1) increase myocardial circulation, or (2) correct mechanical defects resulting from myocardial ischemia, such as left ventricular aneurysm, ruptured papillary muscle, or ruptured interventricular septum.



Fig. 10-26(7). Myocardial sinusoidal space filled by injecting with india ink a human internal thoracic artery.

In the first group, it seems best, from a practical point of view, to list the various procedures under general headings according to the theoretical concept of their intended action and effect. These procedures are as follows.

SURGICAL PROCEDURES DESIGNED FOR THE CORRECTION OF CORONARY ARTERY INSUFFICIENCY

I Extracardiac procedures for pain relief
   A Neurosurgery to block afferent pain pathways
      1 Cervicothoracic ganglionectomy (Jonnesco, 1916)
      2 Chemical nerve block (Swetlow, 1926)
      3 Posterior rhizotomy (Hoven and King, 1942)
      4 Pericoronary neurectomy (Fauteux and Svenson, 1946)
   B Reduction of general metabolism
      1 Total thyroidectomy (Blumgart and Levine, 1933)
      2 Radioactive destruction of the thyroid gland
II Development of collaterals, anastomoses, or both
   A Ligation of cardiac vein (Fauteux, 1940)
   B. Ligation of coronary sinus (Gross and Blum, 1935)
   C Bilateral ligation of internal thoracic artery
   D Epicardiectomy and Ivalon sponge operation (Vineberg)
III Procedures to increase myocardial blood supply
   A. Bypass operations
      1 Myocardial vascularization by extracardiac blood

not been improved by as much as 50 per cent, and this is considered a poor result. The remaining 90 per cent of the patients show a minimum of 50 per cent improvement, and this is considered a good result. Some of the patients (40 per cent) are improved more than 75 per cent, and this is considered as an excellent result. Almost all the patients had sustained infarctions before the operation, and the vast majority were almost completely incapacitated.

In summarizing the surgical treatment of coronary disease and myocardial ischemias, two general principles are involved. One is palliative and consists of neurosurgical procedures. The other is definitive and consists in methods of myocardial revascularization. One of the simplest of these is cardiopexy. The mortality is low, and a 21-year follow-up shows the results are not surpassed by any other method.

In conclusion, it appears evident that the benefits to be obtained from surgery in cases of coronary disease and myocardial ischemia are rehabilitation, protection, and the prolongation of life.

results of these procedures are difficult to evaluate because the neurosurgical reports deal largely with pain, its relief, and neurosurgical techniques Very little is mentioned in regard to the type of condition for which the patient is operated upon.

CERVICOTHORACIC GANGLIONECTOMY. Lindgren treated 105 patients by cervicothoracic ganglionectomy (*operative mortality*, 8 5 per cent). The anterior approach was used in stages 2 months apart; the stellate and upper T_4 and T_5 ganglia were removed bilaterally. Pain was relieved in 75 per cent of patients, with 66 per cent reporting an increased capacity for work. A warning signal still remained. There was no evidence of prolongation of life.

POSTERIOR RHIZOTOMY. This procedure involves section of the posterior sensory nerve roots and of the upper four or five thoracic nerve roots

White reports 31 cases collected from different centers, with 3 *operative deaths*, and with complete relief of pain in all but 2 patients. The advantages of this procedure are the following (1) there is no possibility of regeneration; and (2) the fibers can be cut at both ends at the same operation The disadvantages are (1) it is a major procedure on bad-risk patients, (2) bilateral laminectomy involving four vertebrae, a time-consuming procedure, is necessary, (3) there is danger of ischemia, transverse myelitis, and anoxia owing to the prone position.

PERICORONARY NEURECTOMY. This procedure involves *paravertebral alcohol injection* of the upper thoracic sympathetic ganglia

White has treated 77 patients with precordial pain with 100 alcohol injections, with *no major or serious complications*. He reports that 62 3 per cent of patients experienced complete relief of pain on the side of denervation, 20.8 per cent were improved, 7.8 per cent of the attempts failed, and there was a 9 10 per cent death rate In the hands of others, chemical block of afferent pathways has not been so successful

The disadvantages of this procedure are as follows. (1) it has failed to control pain in at least 10 per cent of cases and there has been an 18 per cent recurrence rate within 2½ months, (2) the injections, started under local anesthesia to detect Horner's syndrome and outline the absence of sweating, may be painful, (3) spinal cord surgery may produce a resultant myelitis; (4) deaths have occurred; (5) intercostal neuralgia may be troublesome and may last a long time.

White suggests use of cardiac denervation for precordial pain in the following groups of patients. (1) those with severe "angina decubitus," to forestall drug addiction and give some relief, (2) those who cannot tolerate hyperthyroidism; (3) those with aortic insufficiency and syphilitic aortitis who have precordial pain.

Certainly the paravertebral injections of alcohol, as carried out by White, seem to be worthwhile in bed-rest patients with severe precordial pain.

Development of Collaterals, Anastomoses, or Both

[illegible] tion [illegible] bilat [illegible]

C[illegible] nary sinus ligation would hasten the physiologic process of aging by the formation of collaterals. Both the procedures of great cardiac vein ligation and coronary sinus ligation in the treatment of coronary artery disease are based *upon this concept.*

Fauteux (1939–1940) reported a protective effect against anterior descending branch ligation after cardiac vein ligation, which persisted up to 1 year in animals; in 1946 he reported his results in 10 patients with precordial pain, 7 of whom had returned to work. Ripstein (1948) analyzed the results of 40 cases and reported that 72 *per cent* of the group had benefited from the procedure.

LIGATION OF CORONARY SINUS. Total ligation of the coronary sinus frequently causes marked venous congestion and turgidity of the ventricular wall For this reason, Beck modified the operation by tying the coronary sinus at its entrance to the right atrium around a 3-mm probe. Beck is of the opinion that by this means, intercoronary collaterals are opened and a wider distribution of blood is brought about throughout the ventricular myocardium. In the past few years, he has performed this operation upon patients suffering from coronary artery insufficiency. The *partial ligation of the coronary sinus* is supplemented by *abrasion of the epicardium and inner surface of the pericardium* with a mechanical abrader and by the introduction of asbestos powder between the heart and the pericardial fat pads that are sutured directly to the heart muscle. This operation is

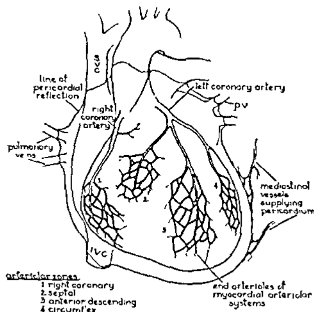


Fig. 10-26(1). Coronary artery distribution into separate arteriolar zones in normal heart.

patients have been known to live without any open coronary arteries whatsoever It is at this level that much clarification is needed

What do clinicians mean when they speak of "collaterals"? The majority of them picture blood vessels, from somewhere, reaching the ischemic areas of the myocardium This view is correct when it is confined to the opening up of communications between neighboring arteriolar zones within the confines of the heart, either upon its surface or within its musculature [Fig 10-26(2)]. It is badly founded when it suggests that extracardiac vessels of arteriolar size are capable of reaching the myocardium Both physiologists and pathologists have drawn attention to the blood vessels that reach the heart in the region of the pericardial reflection around the great vessels as they leave and enter the heart It has been suggested that collaterals may be established between the pericardial blood vessels and the heart via these routes

Evidence for the Presence of Extracardiac Channels. EPICARDIUM [2] The epicardium is composed of a thin layer of mesothelium, a simple squamous or cuboidal epithelium, together with a subjacent layer of fibroelastic connective tissue

CONNECTIVE TISSUE The connective tissue of the epicardium contains a considerable amount of fat, particularly in the region of the sulci and around the layer of vascular channels that lie over the surface of the ventricles It is continuous with the connective tissue forming the serosa of the great vessels entering and leaving the heart The deep layer of the epicardial connective tissue is continuous with the perimysium of the myocardium The perimysium is a dense layer of fibroelastic connective tissue that surrounds groups of muscle fiber bundles. In this layer is a network of blood and lymph capillaries and myocardial sinusoids.

There is thus no doubt that there is anatomic continuity between the capillaries of the serosa of the great vessels and those of the deeper layer of the epicardium. Many injection studies have shown connections between mediastinal vessels and the subepicardial vessels that reach the heart around the great vessels. These mediastinal myocardial-vascular connections have been frequently described, however, they have all been demonstrated by the injection of india ink or other fluid materials, and such injection studies prove very little except that a capillary network of vessels exists between the extracardiac vessels and the coronary vessels [Fig. 10-26(3)].

Of the numerous injection studies made by Schlesinger and Zoll, Blumgart and Zoll, and more recently by May, and others, there is no recorded evidence of arteriolar-size connections between the coronary arterial tree and the mediastinal vessels and the tissues surrounding the vessels that leave and enter the heart of man and animals. This is true of the human heart whether normal and healthy or diseased

The term "collateral vessel," therefore, must be reserved for arterioles that connect coronary arteriolar zones within the myocardium, it cannot be used to suggest the presence of, or the development of, extracardiac coronary arteriolar anastomoses.

The acceptance of this anatomic, pathologic fact makes it clear that *the myocardium can exist only on blood supplied by its own coronary arterial tree*

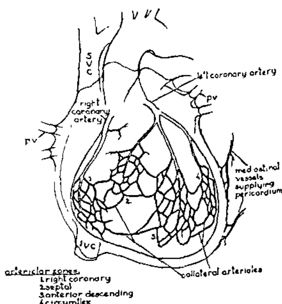


Fig. 10-26(2). Arteriolar collateral development in ischemic heart

[2] See Part 1, Chap. 5 *Editor.*

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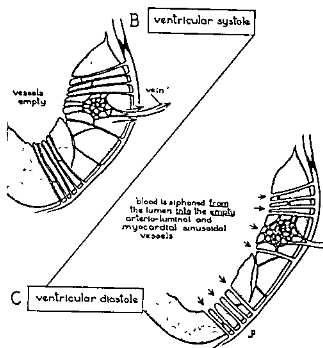


Fig. 10-26(5). Mechanism by which the vascular spaces of the myocardium are emptied and the blood is moved into the venous system

they exist, it has been possible to implant an open and bleeding systemic artery into the myocardial tunnel without formation of a myocardial hematoma. This has been performed many hundreds of times in the author's laboratory using the internal mammary artery. Others have had similar experiences with the splenic, carotid, or subclavian arteries. Such myocardial systemic arterial implants remain open because there is a satisfactory run-off through the myocardial sinusoidal and perhaps arterioluminal channels. A schematic drawing of such a mechanism is shown in Fig. 10-26(6). Figure 10-26(7) shows a myocardial sinusoidal space filled by injecting a human internal mammary artery, 82 hr after implantation, with india ink.

Surgical Pathology of Coronary Heart Disease. In surgery for coronary heart disease, consideration must be given to two major parts of the heart: (1) the part pertaining to the coronary arterial system, which perhaps may best be called *the myocardial circulation;* (2) *the heart itself,* in which the myocardium, the valves, and the papillary muscles may have become damaged.

THE CORONARY ARTERY SYSTEM AND THE MYOCARDIAL CIRCULATION. Atherosclerosis is a major disease affecting the coronary arteries One rarely sees syphilitic aortitis which involves the coronary ostia. There are, however, other causes of coronary artery disease and of myocardial ischemia that are beyond the scope of this article. There is general agreement that atherosclerosis involves the arteries largely in their epicardial courses, leaving a vast arteriolar network within the myocardium comparatively disease-free.

Patients with severe diabetes and hypertension are the exception to the rule. In such patients, the smaller arterioles within the myocardium are much more likely to show atherosclerosis than in other patients without these two conditions

A study of the distribution and extent of coronary artery atherosclerosis reveals that from 13 to 18 per cent of cases examined have segmental disease, i e , isolated areas of occlusion or narrowing These studies have been made at autopsy. It is probable that if more detailed coronary arteriography were available, the incidence of segmental coronary artery disease would be found to be higher, particularly in the younger age group.

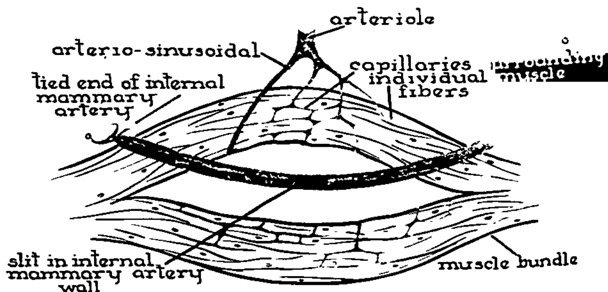


Fig. 10-26(6). Mechanism of internal thoracic artery branching within the myocardium.

cedure by first ligating the arterial blood supply to the lingula; they then painted phenol on the mediastinal surface of the lingula and upon the

they have produced

bronchial arteries to the lingula grow down the bronchus and eventually anastomose with the coronary vessels. This is an intriguing method of revascularization and may prove useful in the treatment of coronary artery disease in human beings.

Pericardial Fat Pad Grafts. In this operation, the medial diaphragmatic and phrenic fat pads are detached from the fibrous pericardium. The epicardium covering the surface of the myocardium is then removed by sharp dissection, and the fat pads are applied to the surface of the heart (Vineberg).

It has been shown by Vineberg et al. and by Martineau that in the partially ischemic heart, arteriolar communication develops between the grafted pericardial fat pads and the coronary circulation. Further, in one patient, 18 months after operation, retrograde injection of the circumflex artery showed the injection mass to enter the diaphragmatic fat pad. Pericardial fat pad grafts, as a supplement to internal thoracic artery implant, have been used by the author since 1953 wherever possible.

It may be that the major benefit derived from the Beck I operation is due to the introduction of extracardiac blood through the pericardial fat pads, which are applied to the surface of the heart after partial ligation of the coronary sinus, instrumental epicardial scraping, and irritation with asbestos powder.

Skin Pedicle and Jejunum Grafts. Other surface grafts, which have been attempted in animals, include a skin pedicle flap, described by Moran et al. (1952), and a jejunum graft, by Key et al. (1954).

Key and coworkers report that in 75 per cent of their cases the jejunal pedicle vessels were open, while in 61 per cent there were anastomoses between the jejunum and the coronary vessels. The type of anastomosis was almost entirely capillary, but they suggest that the amount of blood delivered through multiple capillary anastomoses would equal that produced by several small arteries. Survival from anterior descending branch ligation was 93.1 per cent in grafted dogs, as compared with 26.7 per cent in control animals.

The jejunal graft is probably too major a procedure to be used in the treatment of human beings with coronary artery disease, since it involves, as does cardioomentopexy, an abdominothoracic approach.

ARTERIALIZATION OF THE CORONARY SINUS. Batson (1931) demonstrated that the heart can be kept alive and beating in an isolated state by perfusing it through the coronary venous system. This observation, corroborated by many workers, led to the idea, first described by Roberts et al. (1943), of anastomosing an artery to the coronary sinus, using the subclavian and brachiocephalic (or innominate) arteries.

Beck (1948) reported revascularization of the heart by grafting a systemic artery into the coronary sinus; he then modified it to a two-stage procedure known as the *Beck II operation*.

In the first stage of this operation, anastomosis between the coronary sinus and the aorta is made by means of a jugular vein graft, and a ligature is placed around the coronary sinus just before its entrance into the right atrium. Then, 3 to 6 weeks later, this ligature is partially closed at the second operation. Seven patients with coronary artery insufficiency were operated upon with a high mortality. Bailey modified the procedure and operated upon a comparatively large number of patients. He reports a total experience with 71 patients, 53 of whom had the Beck II operation; there were 8 deaths, and 8 blocked grafts were found at the second stage of the operation. The final results on these patients have not yet been published. Eighteen patients had Kralik's modification of Beck's procedure; again, the mortality and final results are not available.

The Beck II operation has been given up by Beck and by others because of its high mortality and because it was shown (Eckstein et al.) that retrograde perfusion of the coronary bed or through the graft lasts only for about 5 weeks; functional contact with the bed is then lost, probably because of obliterative venous change caused by high arterial pressure in the venous bed.

VENTRICULAR ARTERIALIZATION BY VASCULAR IMPLANTS. The implantation of a systemic artery into the left ventricular myocardium was first attempted by the author (1945).

The internal thoracic artery was detached from the chest wall between the 6th and 4th interspaces, it was divided between ligatures, and the proximal end was buried within a tunnel made in the myocardium. In its new location, the transplanted

2. Surface grafts
   a Pectoral muscle (Beck, 1935)
   b. Omentum (O'Shaughnessy, 1936)
   c. Lung (Lezius, 1937; Carter, 1949)
   d. Lung and ligation of pulmonary artery (Liebow, 1950)
   e. Pericardial fat pad (Vineberg, 1954)
   f. Skin (Moran, 1952)
   g Jejunum (Key, 1954)

B. Arterialization of coronary sinus (Beck, 1948)

C Cardiopericardiopexy
1. Bone, chips, asbestos, etc (*Feil and* Beck, 1937)
2. Talc (Thompson, 1939)

D. Ventricular arterialization by vascular implants
1 Internal thoracic artery implant (Vineberg, 1946–1961)
2 Splenic artery implant (Liebow, 1956)
3. Carotid artery implant (Sabiston and Blalock, 1956)

E. Graft from aorta to myocardium
1 Single (Vineberg and McIntosh, 1954–1957; Sabiston and Blalock, 1956; Smith, 1957)
2 Double (Vineberg and Duchesne, 1957)

IV. Myocardial circulation from the left ventricular lumen
A Epicardiectomy
B. Epicardiectomy and Vineberg sponge operation
C. Direct tapping of left ventricle (Vineberg-Massino)

V Direct attack upon the coronary arteries
A Endarterectomy (May, Bailey, Sabiston, Longmeyer)
B. Endarterectomy with patch graft (Senning)
C. Resection *segments with end-to-end anastomoses* with or without graft (Robb)
D Systemic artery to distal end of coronary artery (numerous workers)

From the above list, it is evident that many different attempts have been made to treat coronary heart disease surgically A careful examination of the experience with each procedure reveals the shocking fact that few of them have had adequate experimental background before their application to human beings The author has frequently stressed the importance of the experimental laboratory in assaying a surgical procedure This view has not been and is still not universally held Yet those who criticize animal experimental evidence *as being valueless because of the differences* between human beings and lower animals are the first to try out a new surgical procedure based on a theoretical but unproved concept It is quite true that that which is of value in an animal may not be of value in a *human being, it is just as true,* however, that a procedure that has not worked in a lower animal is not likely to do so in man.

In the *light of recent knowledge of coronary* heart disease, it is clear that surgical procedures designed for the treatment of this disease should have certain clearly defined objectives and should be based on the known physiologic and pathologic facts.

Objectives of Surgery

1. To relieve precordial pain
2. To relieve right and left ventricular failure
3. To correct mechanical defects produced by myocardial ischemia
4. To increase exercise tolerance and ability to work
5. To prevent further loss of myocardial fibers
6. To prolong life expectancy

Each surgical procedure should be carefully scrutinized to judge whether it is capable of fulfilling the six objectives and is supported by adequate experimental and pathologic evidence.

Neurosurgery to Block Afferent Pain Pathways. INTERRUPTION OF CARDIAC PAIN FIBERS. The following procedures were designed to relieve precordial pain: cervicothoracic ganglionectomy, chemical nerve block, posterior rhizotomy, and pericoronary neurectomy.

When Jonnesco (1916) performed a trial *DI-5 sympathectomy for the relief of precordial* pain, there was little understanding of the mechanism or cause of this type of pain. There never was any question that the circulation in the myocardium would be improved, because it was not until 1928 that the mechanism of pain was clearly explained by Keefer and Resnick. *These authors* crystallized the concept that *precordial pain is due to a relative disproportion between myocardial demand for oxygen and its supply*

Neurosurgeons favor the neurosurgic treatment of precordial pain for the following reasons (1) the cutting of sensory nerves interrupts nerve pathways, (2) severance of motor acceleration nerves interrupts cardiopressor reflexes, (3) cutting of vasomotor nerves theoretically stops vasoconstrictor impulses to coronary arteries, thus permitting development of collateral circulation.

J. C White points out that "all cardiac pain *fibers function* from the upper three or at most four thoracic ganglia to reach the sensorium over the corresponding white rami communicantes, small nerves and their posterior nerve roots" These fibers can be interrupted by chemical injection of *the four upper* thoracic ganglia and their rami communicantes, resection of these ganglia without removal of the sympathetic chain, and interruption *of the upper* four posterior spinal nerve roots. The

time goes on, scar tissue is formed, which prevents the myocardium from maintaining the loosened structure caused by epicardiectomy, thus, the numerous luminal myocardial vascular spaces, which were opened following epicardiectomy, tend to be squeezed closed again by the constricting scar tissue, which develops as the result of the use of asbestos powder. When epicardiectomy is performed, the heart enlarges This enlargement allows the 400-million-year-old arterial luminal, luminal myocardial, and myocardial sinusoidal spaces to enlarge and to siphon blood into their spaces from the lumens of the left ventricle during diastole

When a sheet of Ivalon sponge is placed upon the bared left ventricular myocardium, this sheet tends to keep the myocardium in the same condition as it was at the time of application of the Ivalon sponge. It does not cause contraction, such as that due to the application of asbestos or talc, but rather maintains the status quo.

Direct Attacks on the Coronary Arteries. CORONARY ENDARTERECTOMY. This procedure has been performed on a few patients. Unfortunately to date the mortality has been high and the end results have not been too satisfactory. However, with the introduction of better visualization of segmental coronary artery

artery disease.

Endarterectomy combined with patch graft, as suggested by Senning, seems more promising than endarterectomy alone. It would seem to prevent reocclusion of the artery and offers a better chance for removal of the atheromatous material from the artery and its penetrating branches.

Resection of segments—end-to-end anastomoses, with or without graft—has not been attempted on human beings This is still a laboratory procedure. The introduction of a systemic artery into the distal open end of a coronary artery is likewise a laboratory procedure but may be of value in the future

SELECTION OF OPERATIVE PROCEDURE

It is the author's belief that surgery of coronary artery disease, like surgery of a peptic ulcer, will make use of many methods and techniques Some years ago, surgeons argued as to the best technique for removing the stom-

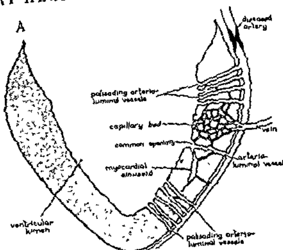


Fig. 10-26(8). Theoretical mechanism of endocardiac nutrition in the ischemic heart after Ivalon sponge operation

ach in the treatment of duodenal ulcer. Their medical confreres were arguing that surgery was of no use as a cure for peptic ulcer. Today there are few who do not admit the value of some form of gastrectomy in the treatment of intractable peptic ulcer. There is no further discussion as to what technique will be used, the surgeon has at his disposal numerous operative techniques and he tailors his operative procedure to suit the peculiarities of the case. Thus, it would seem that the selection of an operative procedure for coronary artery disease will depend upon the pathologic change that has occurred in the particular patient. For example, if, in the near future, it is shown in a young patient that the disease is segmental, very likely endarterectomy will be performed. If the disease is shown to be far advanced, with multiple lesions, one of the bypass operations will be used. Likewise, if the heart is in chronic failure, then it would seem that the Vineberg sponge operation or some modification of this operation, such as tapping of the left ventricle, may be used

However, whichever of these operations is chosen, it is the author's belief that proof should be shown that surgical revascularization has produced channels of arteriolar size between the coronary circulation and the extracardiac source of blood. These anastomotic channels should be large

or longer. The quantity of extracardiac blood de-

known as *the Beck I operation* and is now performed on patients with coronary artery disease in many centers, with reported good results.

BILATERAL LIGATION OF INTERNAL THORACIC ARTERIES. The rationale of the operation is based upon the known presence of capillary-sized anastomotic channels between the pericardiophrenic arteries and the coronary circulation through the pericardial fat pads and pericardial reflections over great vessels. This anastomotic bed is, as has been pointed out, entirely capillary in nature. According to the proponents of this operation (Battezzati et al., 1955), bilateral ligation of the internal thoracic arteries at the 2d interspace increases the rate of blood flow down the pericardiophrenic artery, thus causing blood to flow into the coronary artery bed.

A large series of patients operated upon by different European surgeons, particularly Italian, was reported in Turin, Italy, in which results have been stated to be excellent. However, in no instance has any one of these surgeons showed objective evidence that bilateral internal thoracic artery ligation opened up or developed extracardiac arteriolar-sized channels which communicated with the vessels of the myocardium Although this operation is still being performed and reported in Europe, there is fundamentally no anatomic, physiologic, or experimental evidence to warrant its continued use in human beings Some Russian surgeons have even combined the internal thoracic artery ligation operation with cardiopericardiopexy in the treatment of acute myocardial infarction The results of this operation, as performed in North America and reported upon by surgeons from this continent, have not lived up to early expectations Further, the North American workers, like the European surgeons, have not brought forth any evidence to show that the operation permits extracardiac channels of arteriolar or larger size to develop between the mediastinal vessels and the myocardium

Myocardial Vascularization by Extracardiac Blood. Coronary artery narrowing, resulting in myocardial ischemia, usually occurs in the epicardial parts of the coronary vessels, leaving the arteriolar system lying within the myocardium comparatively intact Surgical revascularization methods attempt to bypass points of coronary artery obstruction by connecting an extracardiac source of blood to the ventricular myocardium distal to these points of obstruction. Theoretically this is a sound concept, based upon the pathologic state that exists in human coronary artery disease. Practically, it has presented most difficult and perplexing problems, particularly in reference to (1) introduction of a volume of blood large enough to relieve myocardial ischemia, (2) equal distribution of the extracardiac blood throughout the myocardium, and (3) maintenance over months and years of the new extracardiac source of blood pathways.

SURFACE GRAFTS. Many types of tissue have been grafted to the surface of the left ventricle in the hope that these grafts would furnish the myocardium with a fresh extracardiac source of oxygenated blood.

Beck attached the left pectoralis major muscle to the surface of the left ventricle This operation has been performed on animals, and on a few human beings, with *questionable results* Many other types of surface grafts have also been employed.

O'Shaughnessy (1936–1937) brought a vascular flap of omentum up through the diaphragm and affixed it to the anterior surface of the left ventricle, where it formed anastomotic channels between the vessels of the omentum and the heart Of 12 patients operated upon, 8 survived, 7 of the survivors continued to show increasing improvement. This operation has been performed twice by the author, without beneficial results but without mortality One of the two patients had many gastrointestinal tract disturbances (*this apparently is one* of the complications experienced by O'Shaughnessy's patients). In addition, this operation has *been criticized* because of its combined abdominothoracic approach and because proper visualization of the pathologic changes in the heart cannot be achieved It is no longer employed clinically.

Cardiopneumopexy. Lezius (1937) used the lower and middle lobes of the left lung and grafted them to the myocardial surface in animals. This method of myocardial revascularization was further explored by Carter et al.

Both Lezius and Carter demonstrated blood vessel channels between the pulmonary and coronary vessels, but information concerning the direction of blood flow, the volume of blood delivered through the new channels, and the duration is not available This method has been criticized by Ghinst because it can deliver only unoxygenated blood, he further stated that the pulmonary vessels communicated with myocardial venous, not arterial, channels Carter used this method in the treatment of coronary artery insufficiency in two patients, one of whom died, the other is said to have done well. Liebow et al modified this pro-

ponge operation may be helpful. However, if the left ventricle is enlarged because of severe hypertension, it is questionable, because of numerous diseased arterioles within the myocardium, whether the patient should undergo any form of revascularization surgery.

RAPID PROGRESSIVE DETERIORATION. Many surgeons prefer to wait for some degree of stabilization in these patients Not infrequently, the augmentation of precordial pain may be a precursor of coronary artery thrombosis and infarction Such patients may die in the anesthesia room, on the operating table, or shortly thereafter, from an exacerbation of their disease.

MALIGNANT HYPERTENSION, SEVERE DIABETES, OR OTHER INCURABLE DISEASES

THE "ANGINA DECUBITUS" GROUP. This group consists of patients who suffer pain at rest without exciting cause Patients who experience night pain or pain at rest while watching television or after eating, do not necessarily have angina decubitus Patients with true angina decubitus should not undergo revascularization surgery, the mortality is high and the end results are poor in those who survive operation Pathologic examination of the hearts of patients who have died from angina decubitus reveals that such patients generally were living with one pin-point opening, or perhaps two, in their major coronary arteries There is insufficient coronary circulation to carry such patients through anesthesia without left ventricular failure, ventricular fibrillation, or a fresh coronary thrombosis within 3 weeks of surgery. Further examination of such hearts shows that, because of the prolonged period of ischemia, which in the author's series was well over 10 years, there is little myocardial muscle fiber left to revascularize

The view that surgery is contraindicated for patients with angina decubitus has been queried by some, who are unwilling to suggest surgery to patients with less advanced disease, still able to get along with an occasional nitroglycerin tablet This is similar to suggesting that a patient with mitral stenosis who is doing well on digitalis does not require mitral commissurotomy Unquestionably such patients do well for a while without commissurotomy, but it is well known that the death and complication rate of patients with mitral stenosis mounts steadily with each succeeding year that surgery is postponed The same is true of coronary heart disease The longer the disease process is active, the greater the danger for the patient

The recent report of White et al. on a 25-year follow-up of patients with myocardial infarction can be used as a guide in the selection of patients for revascularization surgery. To quote these authors: "The best aid to long term progress following myocardial infarction is the degree of recovery of the patients following the acute period of illness." In their patients who had complete medical recovery following infarction, 82 per cent were alive at the end of 5 years, whereas of the entire group of 162, only 49 per cent were alive 5 years after myocardial infarction

Although patients with precordial pain without infarction appear to have a better future, White states that the mortality in patients with coronary disease who have pain is usually 7 per cent above the expected mortality. *The asymptomatic patient, therefore, has a better prognosis*, the hearts of such patients being well taken care of by their undiseased "good-neighbor" arteries, which are known to send collaterals to the ischemic zone, so that there is no need for extracardiac sources of blood. Any type of revascularization surgery upon such patients can do no more than nature has already done

PREOPERATIVE INVESTIGATION AND POSTOPERATIVE CARE

Diagnosis. Preoperative investigation is absolutely essential, in order to establish a firm diagnosis and to ascertain the presence or absence of other disease or condition that might be the source of the patient's symptoms

In general, *chest pain* that is not initiated by physical activity or emotion and does not disappear rapidly with rest should be regarded with suspicion. Generally, a pain of long duration that is not made worse by exercise and is not relieved by nitroglycerin, is *not* caused by myocardial ischemia A search for hiatus hernia, biliary tract disease, peptic ulcer, and even cervical or upper thoracic disks may disclose the source of the pain The ECG is of value when it is positive. Failure to obtain electrocardiographic evidence of coronary artery disease with the Master's two-step test or the treadmill exercise may leave the diagnosis in doubt

vessel remains open because of side branches which are left open at the time of implantation and which bleed into vascular spaces surrounding the internal thoracic artery within the tunnel. The implanted vessel commences to bud at the end of 12 days, and, between 3 and 6 weeks, it sends out numerous arteriolar or larger branches which anastomose with the surrounding arteriolar network lying within the myocardium. When these thoracic-coronary anastomoses occur, which they do in 94 per cent of canine hearts made ischemic by ameroid constrictors placed on the coronary vessels, systemic arterial blood is propelled from the subclavian artery down the internal thoracic artery into the myocardial arteriolar network. There, it is distributed at first to the anterior portion of the myocardium and then, gradually, over a period of 5 months, as the ischemia progresses, to the entire left ventricle. Through these thoracic-coronary anastomoses, a rate of blood flow into the heart as high as 55 ml/min has been measured.

Sixty per cent of the arterial blood introduced through the internal thoracic artery 5, 6, and 7 months after implantation has been recovered from the coronary sinus, indicating that blood introduced through the implanted internal thoracic artery reaches the ventricular myocardial fibers.

It has been shown, both in animals and in man, that if there is myocardial ischemia, the implanted vessel, studied 6 months to 3 years after implantation, has remained patent and does not close off by intimal proliferation.

Many other workers obtained similar results with internal mammary artery implantation when the techniques outlined by the author were carefully followed. More recently, similar results have been obtained by Liebow, who implanted *the splenic artery* into the myocardium, and by Sabiston and Blalock, who have implanted *the carotid artery* in animals. Others, including the author, have used in animals the same principles to implant free homologous arterial grafts, which are attached at one end to the aorta Smith has substituted homologous grafts for nylon tubes, and has performed a nylon tube implant in human beings with coronary artery disease

The principle of internal mammary artery implantation is based upon two pathologic facts: (1) that coronary artery disease involves mainly the epicardial branches and, in particular, the first 3 to 4 cm of the origin of the main vessels; (2) that extensive intercoronary arteriolar anastomosis is present when myocardial ischemia develops because of coronary artery stenosis. Thus, the internal mammary artery, or any other vascular implant, bypasses the points of coronary artery obstruction to pour systemic extracardiac arterial blood into the ventricular myocardial arteriolar network. Once there, because of collateral arteriolar branches, the blood should reach all parts of the left ventricular myocardium.

Many hundreds of animals have undergone internal mammary artery implant, and well over 100 patients with coronary artery insufficiency have thus been treated The results have been most encouraging and will be discussed below.

Myocardial Circulation from Left Ventricular Lumen. The early, primitive reptilian creatures had no coronary arteries. The hag fish, which still swims in the South Pacific ocean, a 400-million-year-old prehistoric creature, has a systemic heart in which there are no coronary arteries and no nerve supply: the myocardium of the systemic heart receives nutrition through channels which communicate with the lumen of the ventricle. The mechanism of the myocardial circulation is that of ebb and flow, similar to a bathroom sponge being squeezed and relaxed. In our laboratory, we have been able to show that a beating heart in the animal can and will siphon Schlesinger mass from the left ventricular lumen when its two major coronary arteries are cut if it has had a previous epicardiectomy or an epicardiectomy plus the Vineberg sponge operation

Experience with patients undergoing the Vineberg sponge operation has disclosed that (1) the [illegible]

(3) these hearts enlarge These three facts suggested that the beating, ischemic left ventricle of the human heart, in the presence of occluded, or nearly occluded, coronary arteries can and does siphon blood from its own left ventricular cavity after removal of the epicardium [Fig 10-26(8)] These experimental and clinical observations become extremely interesting if an analysis is made of some of the operative procedures that have been used in the treatment of coronary artery insufficiency Thus, we find that in the Beck I operation, which has a good record of satisfactory results, the first stage is epicardiectomy, followed by partial ligation of the coronary sinus, and then by the application of pericardial fat pads to the left ventricular myocardium; before this is done, asbestos powder is sprinkled over the surface of the heart. The sprinkling of asbestos powder, in the author's belief, negates the value of the epicardiectomy. as

ferent results may be expected from revascularization surgery. These are (1) patients with angina decubitus (i e , pain at rest without exciting cause), and (2) patients with no pain at rest. Until objective radiologic evidence of improved myocardial circulation after surgery is available, the observer must rely upon the following criteria as indications of improvement: (1) survival, (2) disappearance of precordial pain for more than 6 months, (3) increase in work and exercise tolerance, (4) improvement in the ECG, and (5) failure to develop fresh infarction

Survival. This pertains to both postoperative and long-term survival The American College of Surgeons has defined the period of postoperative survival as the 30 days immediately after the operation Death during this period, no matter from what cause, must be recorded as a postoperative death

Dana and Ohler found a 7 per cent mortality of cardiac origin in patients who had suffered from pain at the time major surgery was performed. The same authors point out that there was no mortality of cardiac origin in patients with previous myocardial infarction who were asymptomatic at the time of major surgery, whereas the mortality was 40 per cent in a small group of patients who had had recent infarctions Patients with coronary

tality above this figure fundamentally represents the true operative mortality for any given procedure

Disappearance of Precordial Pain. Pain is subjective and thus very difficult to estimate both before and after operation For this reason, the author's patients are seen by two cardiologists and a psychiatrist Certainly, the disappearance of pain [illegible]

that an attempt to evaluate the effect of an operative procedure should not be made less than 6 months after the operation

Increase in Work and Exercise Tolerance. In order to measure the improvement after operation, a careful record is made of the patient's ability to work and exercise before operation Accurate questioning gives some indication of his ability as to exercise, e g , the question, "How far can you walk in your town at the same pace as the crowd on the street?" invariably brings out that the patient may be able to walk a half-mile or so, but at a very reduced pace The Master's two-step test and the

treadmill, [illegible] permit a much more dependable estim

Improv

sults obta

much to [illegible]

ECG has frequently failed to show evidence of improvement when the animal's exercise tolerance has returned to normal and when, later, autopsy findings have proved satisfactory myocardial vascularization. One should not place too much reliance on the ECG in estimating postoperative improvement or lack of it.

Failure to Develop Fresh Infarction. Revascularization surgery does not alter the predetermined course of coronary artery disease except to prevent myocardial fiber loss Thus, coronary artery occlusion may and does sometimes occur after a revascularization procedure.

Evidence is now accumulating to indicate that coronary artery occlusion may occur without evidence of myocardial infarction following a satisfactory revascularization This appears to have been true in at least five cases in which internal mammary artery implantation was performed.

There are three operations in use in the treatment of coronary artery disease in human beings which have had a most extensive experimental background and a long period of clinical trial. They are (1) the Beck I operation; (2) the internal mammary artery implantation (Vineberg); and (3) the Vineberg sponge operation.

The Beck I operation has a low over-all mortality, the good results are most impressive Brofman reports 400 patients operated upon with an operative mortality of 5 per cent and a late mortality of 15 per cent. One hundred and ten of these patients were followed 3 to 5 years; the results were as follows:

Condition	*Percentage*
Excellent (little or no pain, working full time, no subsequent heart attacks)	39
Good (occasional heart symptoms, working more than before operation)	31
Fair (little apparent improvement)	6.4
Poor (no apparent benefit)	1 8
Died during operation	5
Died later	15
Total	98 2

It should be noted that of the 110 patients, 45 had severe precordial pain, 45 had moderate pain, and only 20 showed mild symptoms before opera-

livered to the myocardium through the anastomotic channels should be sufficient to relieve myocardial ischemia at rest and under stress. The patient should survive without infarction after ligation of one or more major coronary vessels. Removal of the extracardiac source of blood after ligation of the anterior descending branch should result in death or infarction. Coronary artery sclerosis and occlusion should be produced and should be treated by the introduction of a fresh extracoronary source of blood. Blood flow measurements and oxygen-consumption studies should be made in order to determine the amount of blood and oxygen delivered to the heart. Anterior and circumflex coronary arteries should be gradually occluded as a means of producing left ventricular ischemia, and an evaluation of the revascularization procedure in the protection of the myocardium should be made under such conditions.

An operative procedure that experimentally fulfills the above criteria should theoretically be capable of attaining the following objectives, which, as pointed out earlier in this chapter, form the basic aim in treating coronary artery disease by surgical means (1) relief of precordial pain, (2) increase of exercise tolerance and ability to work, (3) prevention of further myocardial fiber loss, (4) prolongation of life expectancy, and (5) low operative mortality

A careful study of the various surgical procedures that have been outlined reveals that at present only three of them have extensive laboratory proof of value These are the Beck I, the Vineberg internal thoracic artery implantation, and the Vineberg sponge operations

SELECTION OF PATIENTS

In 1950 the author, like other surgeons in the field of coronary artery surgery, was given no opportunity to select patients Cardiac surgery, of any type, was considered highly experimental and extremely hazardous The only patients reporting for surgery were desperate, disabled, and pain-ridden persons, a large percentage of whom were bed-chair invalids Experience showed that the proper selection of patients for surgery should depend largely on the stage of development of the patient's disease, and the following criteria were agreed upon.

Indications for Surgery. PROVED CORONARY ARTERY DISEASE, WITH TYPICAL PRECORDIAL PAIN. The presence of proved coronary artery disease in itself is not sufficient indication for surgery unless the patient suffers from precordial pain which is truly causing difficulty. The author and his medical associates are firmly convinced that the occurrence of occasional precordial pain after unusual physical effort or excitement does not warrant a major surgical operation. Such a patient should be advised to forego the extra nine holes of golf. This point of view, however, is not subscribed to by Brofman and Beck, who believe that the presence of coronary artery disease in itself is an indication for surgery, even though the patient may be asymptomatic.

FAILURE TO IMPROVE ON MEDICAL TREATMENT OVER A PERIOD OF 1 TO 2 YEARS The question is: If one does not operate upon a patient with coronary artery disease who is asymptomatic, or who has occasional pain only, at what stage in his disease should surgery be performed? There is a great divergence of opinion on this point. The author's group, however, has elicited evidence that would seem to indicate *that operation should be performed on those patients who have failed to show improvement and whose pain causes disability after an adequate medical regime of 1 to 2 years' duration*

TWO CORONARY OCCLUSIONS WITH MYOCARDIAL INFARCTION. Patients who have had two or more coronary artery occlusions with infarction, even though they may be asymptomatic, have such a poor outlook for survival that some cardiologists are of the opinion that they should be accepted for surgery.

VENTRICULAR FAILURE, RIGHT AND LEFT, WITH OR WITHOUT PRECORDIAL PAIN.

Contraindications for Surgery. ASYMPTOMATIC CORONARY ARTERY DISEASE. As mentioned above, not all investigators consider this a contraindication.

RECENT INFARCTION, OR EVIDENCE OF DISEASE ACTIVITY Most cardiac surgeons and cardiologists are agreed that a period of 6 months should elapse after infarction before surgery is considered. This view, however, is not accepted by all. Smith operated, with what appeared to be a good result, on a patient who had had two recent myocardial infarctions.

MARKED ENLARGEMENT OF THE LEFT VENTRICLE The enlarged left ventricle may represent dilatation due to failure, hypertrophy due to myocardial ischemia, or a combination of both. In any of these cases, the Vineberg

it to a femoral artery. Two of the 3 patients survived the procedure, 1 of them died 10 days later from a fresh coronary artery occlusion and infarction

There is considerable disagreement at present as to the best means of bringing about circulatory assistance in cases of coronary artery shock. Some subscribe to the principle outlined by Dennis and his group, who indicated that a good result can be obtained by using the pump-oxygenator Others feel that this technique hinders rather than helps the failing heart; this opinion, however, has been based on experience in the experimental laboratory, which is not comparable with experience in human beings, where there is failing circulation because of a failing left ventricle.

Some investigators have suggested that circulatory assistance in coronary artery shock be provided by passing a catheter through the superior vena cava into the left atrium through the interatrial septum, thus withdrawing the blood from the left atrium and passing it into a heart-lung machine and back into a femoral artery. *Left heart bypass* is suggested to relieve the left heart of any strain. This procedure has been carried out, to the author's knowledge, in one patient in Sweden, but unfortunately the patient died. The future of circulatory assistance in coronary shock is certain to be great.

Roentgenology. During the past few years, it has become possible to outline the coronary arterial tree. It is the author's opinion that in all patients being considered for surgical treatment of coronary artery insufficiency, the degree and location of occlusion of the coronary arterial tree should be outlined by one of the numerous techniques now available. Only by *coronary arteriography* is it possible to decide whether the patient has any coronary artery disease. Frequently in the author's clinic, patients have had clinical histories strongly suggesting that they were suffering from coronary artery insufficiency; yet the coronary arteriogram has failed to show any evidence of disease. Such patients have not undergone any form of surgery.

It is the author's belief that if one coronary artery is narrowed but two major coronary arteries are free of disease, the patient will probably develop intercoronary collaterals, which will bring blood from the normal coronary arteries into the area supplied by the narrowed diseased vessel. If such a patient fails to improve clinically, one should resort to operation not only to introduce extra blood but also to cause a good distribution of the blood that has been introduced through the two good coronary arteries

If two major coronary arteries have been narrowed to an average cross-sectional area of 50 per cent or more of their combined luminal areas, a point of critical narrowing has been reached, and the patient, in the author's opinion, is in danger of ventricular fibrillation or myocardial infarction Such patients should undergo surgical intervention, and the operation must be designed to suit the particular condition in the individual heart under consideration

Blood Pressure. Blood pressure should be taken four times daily and once at night, so that an average blood pressure level may be established.

Fluid Balance. Preoperative daily intake and output measurements when averaged form a sound base line for the amount of postoperative fluid to be administered.

Operative Care. The patient with coronary disease is usually apprehensive. For this reason, care should be taken to see that he is under deep sedation and is not taken to the operating room until the anesthetist is ready to start the anesthesia. Substernal pain prior to operation, when not relieved by nitroglycerin, may reflect a new occlusion with infarction and is a contraindication to surgery. Such patients should be returned to bed and watched for at least 1 week. The surgeon should ask the patient in the anesthesia room if he has precordial pain, if such pain is present, the operation should be postponed During the induction of anesthesia and the operation, the blood pressure must be maintained with Neosynephrine drip, which may be administered through a cut in the foot or arm. To avoid excess fluid, the Neosynephrine solution is strengthened as needed, starting with 5 ml Neosynephrine per 500 ml of 5 per cent glucose and water. It is advisable to insert a Wangensteen tube into the patient's stomach after induction of anesthesia to prevent gastric pressure on the heart postoperatively and to prevent paralytic ileus, which sometimes develops postoperatively.

Postoperative Care. The most important factor in postoperative care is to maintain the blood pressure at average preoperative levels Failure to do so favors cerebral and coronary thromboses.

Early ambulation is encouraged after certain types of operation, but after the internal mammary artery implant procedure, in which the pericardium is left open, movement is not permitted for 48 hr. After any coronary surgery, the patient has to live upon his own inadequate coronary circulation until extracardiac sources of blood can reach the myocardium. He should therefore be treated as though he had had a coronary artery occlusion with infarction, and should be given 4 to 6 months of convalescence to permit the new vessels to grow large enough to be of real value

Anticoagulant Therapy. The author and his coworkers have used anticoagulant therapy, by oral administration, starting on the second or third postoperative day. The value of this therapy in the treatment of coronary artery disease may be questioned, but it may be helpful in preventing thrombosis initiated by operation and bed rest.

RESULTS

The treatment of coronary artery disease is probably one of the most difficult to evaluate because of the numerous and unpredictable variations that occur during the natural course of the disease This is true for both medical and surgical therapy The comparison of individual cases is difficult, it is not so difficult, however, to compare groups of cases that fit into a certain broad classification. Such a basic classification has been established, and with excellent effect, for the surgery of mitral stenosis.

In the author's experience, there are two main groups of patients in which entirely dif-

10

The surgery of ventricular aneurysms

HOUCK E. BOLTON AND CHARLES P. BAILEY

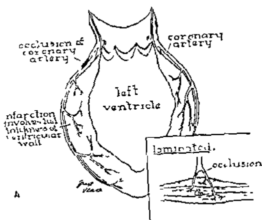
An aneurysm of the ventricle of the heart may be defined as a more or less localized outpouching of the continuity of the wall of the ventricular chamber Such aneurysms may be the result of a congenital malformation (so-called diverticulum), accidental or surgical trauma, or degenerative changes in the muscle fibers (postinfarctional)

The first recorded case of ventricular aneurysm was reported by Hunter (1757) The first operative attack upon such a lesion was made inadvertently by Sauerbruch (1937) While attempting to remove a mediastinal tumor, he made a limited incision into such an aneurysmal sac, allowing palpation of the interior of the ventricular chamber This cardiotomy incision was closed by simple suturing of the opening

Deliberate suture plication and constriction of the base of an aneurysm sac in order to decrease the size of the lesion was described by Beck (1944) More recently, D'Allaines reported a case in which a similar principle was employed Actual resection of a ventricular aneurysm was first attempted by Glover (1953) Using a somewhat different technique, Bailey (1954) performed a subtotal resection of a postinfarctional type aneurysm with survival Since that time, eight additional patients have been treated similarly with but one death

ETIOLOGY

The development of a *diverticulum of the ventricle* is believed by Drennan and V... de ...s of ... The ... any unusual increase in intraventricular pressure occur during prenatal development



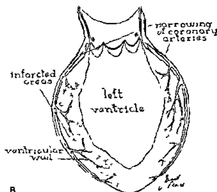


Fig. 10-27 A. Acute myocardial infarction involving full thickness of ventricular wall is shown in comparison to the laminated type of acute myocardial infarction which involves a layer of muscle in the myocardial wall. B. Chronic myocardial infarction demonstrating spotty irregular areas of myocardial fiber death and replacement by scar tissue.

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In the author's experience, there are two main groups of patients in which entirely dif-

tion and, to a degree, impedes filling from the left atrium—similar to the dysfunction associated with aortic regurgitation

DIAGNOSIS

Patient Selection. The symptoms, signs, and electrocardiographic changes associated with ventricular aneurysms may provide only a suspicion of its presence. An abnormal bulge in the x-ray silhouette and a paradoxically pulsating mass seen along the heart border by fluoroscopic examination are observed in most cases (Fig 10-28A) Those patients having an actual paradoxic movement of the wall or having signs of chronic heart failure following a history of myocardial infarction should be studied by roentgen- or electrokymography or, preferably, by opacification of the ventricular chamber. Such opacification by a contrast medium, such as 70 per cent Diodrast or 90 per cent Hypaque, is now done by direct ventricular puncture in preference to left atrial injection. Serial radiographs demonstrate the changes in size with systole and diastole and confirm the site of origin from the ventricular chamber (Fig. 10-28B, C).

Nonvisualization of the lumen of an attached aneurysm by such a method of examination may suggest that the sac contains soft thrombotic material. Paradoxic motion is not observed in these cases. Anticoagulant therapy to preclude embolization may be used in such a case in preference to surgical methods. If treated medically, anticoagulant therapy

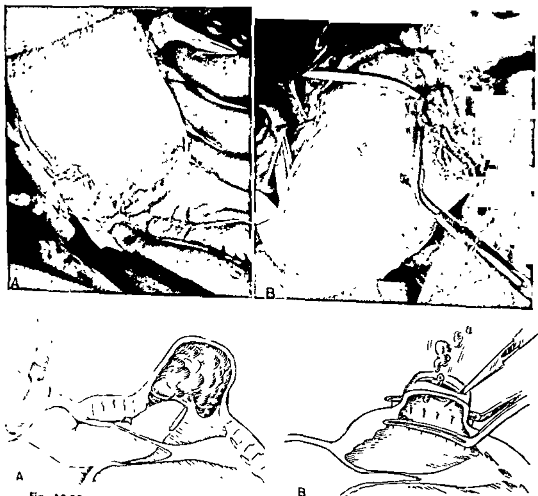


Fig 10-29. A Diagram demonstrates digital exploration of the aneurysm through the appendage and mitral valve The photograph shows the intact aneurysm. B. The *diagram* shows the method of "flushing out" contained *thrombi*, prior to closing the clamp. The photograph shows the clamp applied to the base of the aneurysm.

tion. The patients who died later had an average preoperative duration of symptoms of 4 years. Forty per cent of the patients had two or more episodes of acute myocardial infarction before operation. Brofman reports that 20 per cent of the patients had left ventricular enlargement but only a few had evidence of any congestive failure.

Hill has surveyed the results of the first consecutive 36 patients who underwent internal mammary artery implantation at the Royal Victoria Hospital. Figures have been compiled by Hill on the basis of a 5- to 9-year follow-up. The operative mortality for this group was 13 per cent, on the basis of the author's experience, 4 of the 5 patients who died in this series would not be operated upon today. The 5- to 9-year study of the 31 patients who survived the operation showed marked improvement in 67.7 per cent of them. In this group, 7 per cent had complete pain relief within the first 9 months. As time passed, an increasing number of patients became pain-free, until at the end of 3 years 37 per cent of the group were completely free of pain. Some 75 per cent of these patients had been disabled before surgery, 72 per cent returned to work after surgery. *The combined Vineberg and Walker series of 110 patients with coronary artery disease treated by internal mammary artery implantation showed that the over-all mortality rate for the two series for patients who had had no pain at rest was 5.8 per cent.*

In the group of 110 patients in which there was no precordial pain at rest, 72 per cent were totally disabled prior to operation. Most of the patients could walk approximately one-half a city block prior to operation. After the operation, over 78 per cent had no pain or had less pain, and 79 per cent returned to work.

The Vineberg Sponge. This operation has been used in the past 3 years with considerable success in the treatment of patients over 60 years of age, those with ventricular hypertrophy and those with chronic left and right ventricular failure. The internal mammary artery implantation and the Beck I operation have been reserved for patients with no precordial pain at rest without exciting cause and with small left ventricles.

Patients with chronic ventricular failure who had been digitalized and "dried up" before operation, in general withstood surgery quite well, the operative mortality for a group of 24 patients was less than 8 per cent. In the entire group, 22 individuals had had previous infarction and 21 had chronic ventricular failure (right, left, or both). Twenty-nine patients were suffering from precordial pain, and 19 were unable to work. Following surgery, 15 patients were pain-free and 18 improved markedly.

SURGERY OF LESIONS OF THE HEART RESULTING FROM CORONARY ARTERY INSUFFICIENCY

In the operating room, the author has encountered two unsuspected cases of *right ventricular aneurysm.* Both cases were treated by the Ivalon sponge procedure. There are, however, in the literature, reports of *left ventricular aneurysms* that have been successfully treated using extracorporeal circulation, by resection of the aneurysm and resuturing of the cut surfaces of the left ventricle.

When the aneurysm is saccular, the incision is small, when the aneurysm is large and fusiform, a very large portion of the ventricle has to be resected and usually a considerable quantity of intraventricular thrombus must be removed. Usually patients with this condition come to the attention of the surgeon following two to three previous infarctions and because of left ventricular failure. Recently, the author resected a left ventricular aneurysm which involved the entire anterior surface and a good part of the lateral surface of the left ventricle. The incision measured over 20 cm in length. The patient was in chronic left ventricular failure following three myocardial infarctions. The aneurysm extended out to the chest wall in the midaxillary line. Resection was carried out without difficulty, using extracorporeal circulation, and the patient had an uneventful postoperative convalescence.

The *ruptured intraventricular* septum following myocardial infarction has likewise been repaired with success in a few instances using extracorporeal circulation. Some of the patients have died later from another attack of myocardial infarction, but at autopsy, the repaired intraventricular septum has been shown to be unchanged.

Ruptured papillary muscles usually occur because of rupture of a lateral papillary muscle which results in mitral insufficiency. *A few patients with this condition* have been operated upon, and the mitral insufficiency has been di-

re[illegible]

ni[illegible]

a word concerning circulatory assistance in the treatment of *coronary artery shock.* The usefulness of circulatory assistance in the treatment of coronary artery shock was first reported by Dennis, who used a pump-oxygenator, removing blood from a femoral vein and returning

tained thrombi is provided by wide incision of the aneurysm. Hemostasis is restored promptly by the application of a special clamp designed to prevent slippage from the neck of the sac (Fig. 10-29B). Postoperative embolization may be prevented by anticoagulant therapy.

SURGICAL TECHNIQUE

Although Beck advocated reduction in size of these aneurysms by reenforcement with fascia lata, this type of procedure would seem to be inadequate and perhaps hazardous in the presence of intraluminal thrombosis. Complete excision of the sac, as undertaken by a number of surgeons, has been followed by a fatal outcome in some cases These deaths have been attributed to embolic episodes or to the persistence of intractable heart failure following the surgery. Experimental work suggests that reduction in the diastolic capacity of the underlying ventricular chamber may precipitate chronic heart failure The type of circulatory obstruction produced by ventricular resection in dogs appears similar, functionally, to that which is observed in experimentally produced mitral stenosis. Postoperative compensatory dilatation of the ventricle was not observed in the authors' experience

The currently employed method of ventriculoplasty avoids both the threat of embolic episodes and the chronic heart failure because of a wide resection with reduction in left ventricular filling capacity The aneurysmal sac is "tailored," so that expansion is prevented and so that the heart is changed to one of optimum shape and efficiency. The thin apical portion of the sac is resected, while the strong basal portion is utilized to construct a secure fibrous wall of the ventricle (Fig 10-30) If a papillary muscle takes origin from the wall of the sac, it may be included in the clamp and suture line The normal valvular supports will remain unchanged, and mitral incompetence will not be created

A special multitoothed clamp is applied across the base of the sac immediately after the fundus of the aneurysm is opened. This allows the intraventricular pressure to eject any thrombotic material before the clamp is closed completely. This precaution has seemed to prevent systemic embolization.

TABLE 10-2. RESULTS OF OPERATION

Type of aneurysm	*No of cases*	*No. of deaths*	*Cause of death*
Congenital	1	0	0
Posttraumatic	2	0	0
Degenerative	6	1	Systemic embolization

The surgical problem is significantly altered in false aneurysms following trauma or surgical incisions The actual size of the left ventricular chamber may remain unaltered, and the ventricle most frequently communicates with the aneurysm through a small fistula. Excision of the sac with suture repair of the communicating opening has provided a permanent correction.

The results of excision in congenital diverticula have been excellent The cases discussed include one such patient. Excision was accomplished by clamping the base of the sac and by simple suture. However, in the treatment of the postinfarctional aneurysm, results have been generally less satisfactory. Using the tailoring principle of ventriculoplasty, five patients have survived The death reported in this group was due to dislodgment of an attached mural thrombus with systemic arterial embolization This accident may be avoided by the "flush-out" technique as described above. The remaining patients in this group have attained an excellent postoperative result, with the exception of one patient who developed a second aneurysm.

The posttraumatic aneurysms encountered followed previous heart surgery One of them occurred through the weakened cicatrix at the site of a ventricular tear produced during mitral commissurotomy The other occurred through a ventricular scar due to transventricular aortic commissurotomy These aneurysms were treated by simple suture of the defect in the ventricular wall, with a good postoperative result in each case.

PART II

Disturbances of the heart rate and rhythm; excitability and conduction disturbances

Posttraumatic aneurysms will undoubtedly become more common. The advent of cardiac surgery has introduced the necessity of many ventriculotomies, and one must assume that a very small percentage of such procedures will be followed by a weakened area of the myocardium. Other types of accidental injuries likewise provide a possible source of aneurysmal lesions.

The most common cause of ventricular aneurysm is the myomalacia which follows *acute coronary arterial occlusion*. On the basis of Master's estimated incidence of myocardial infarction, it is believed that between 25,000 and 200,000 new cases of ventricular aneurysm develop annually in the United States alone. These aneurysms, unfortunately, are frequently overlooked.

PATHOPHYSIOLOGY

As the entire thickness of the myocardium is involved in large infarcts, most of the muscle fibers are destroyed and undergo liquefaction necrosis The central portion of the infarct heals much more slowly than does the periphery. Should undue strain be placed upon this area during the healing phase, the thin central portion may bulge outward into a noncontractile paradoxically expansile pouch Since the aneurysm develops initially from a large area of myomalacia, it becomes sessile with no true neck. The overlying pericardium becomes adherent and markedly thickened, thereby preventing rupture after the initial healing has begun.

An aneurysm exerts an extremely deleterious effect upon the ability of the ventricle to maintain an adequate net stroke output. Because of its semielastic nature, the wall of the sac stretches during systolic contraction of the ventricle, producing a paradoxic pulsation during systole. The dysfunction produced is similar to that present in mitral regurgitation. A certain portion of the ventricular content is wasted since it is not expelled into the aorta During diastole, the sac collapses, emptying its contained blood into the chamber of the ventricle This produces left ventricular dilata-



Fig. 10-28. A. Posteroanterior and lateral roentgenogram in a 42-year-old white male showing a true ventricular aneurysm with a small neck. B Contrast visualization by direct injection of 70 per cent Diodrast into the left ventricle C. Postoperative contrast visualization roentgenogram showing an essentially normal cardiac chamber.

PART II

Disturbances of the heart rate and rhythm; excitability and conduction disturbances

should be planned for the patient's entire life span, or until such a time when the aneurysm and its contained clot may be eradicated.

Since most of these patients present a history of one or more myocardial infarctions, it must be assumed that some degree of damage exists even in the remaining "normally functioning" myocardium. These patients are poor surgical risks. Surgical intervention should be deferred until 6 months after the last coronary occlusion. This period of healing will provide adequate time in which dense scarring may be formed about the neck of the aneurysmal sac. Excision should be recommended only when paradoxic motion can be demonstrated by kymography, fluoroscopy, or ventricular opacification. This is substantiated by a review of postmortem studies of aneurysms. Rupture of a postinfarctional aneurysm seldom occurs The mechanism producing death is usually congestive failure—related to the mechanical inefficiency produced by the presence of the semielastic sac. More infrequently, contained thrombotic material may become detached and result in peripheral embolization

During the surgical procedure, certain steps are essential to prevent systemic embolization. Intracardiac exploration by way of the left auricle and the mitral valve provides an accurate method for the recognition of mural thrombi about the neck of the sac (Fig 10-29A). Complete external flushing of con-

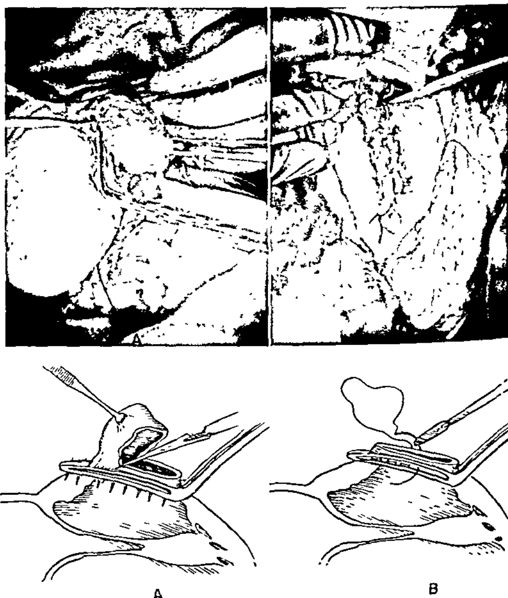


Fig. 10-30. A. The diagram and photograph show the actual excision of the redundant aneurysmal wall. B. The diagram demonstrates the first line of sutures being placed through the clamp's fenestration. The photograph shows the completed suture line after removal of the clamp.

1

Disturbances due to modified function of the sinoatrial node

ALDO A. LUISADA

SINUS TACHYCARDIA

Cause and Types. The most common sinus tachycardia is caused by *exercise* It lasts for a long time if the heart muscle is weak

Digestion is often accompanied by increased heart rate This occurs if the quantity of food and drink is too great or if the heart muscle is weak The ingested fluid increases the volume of circulating blood, thus increasing cardiac strain

Assuming the erect position is accompanied by an increased heart rate because of decreased intensity of carotid sinus reflexes *Emotion* is accompanied by tachycardia. Many *drugs* and *poisons* also cause tachycardia Among them, caffeine and nicotine are the most commonly used *Fever is usually accompanied by rapid* heart action

Endocrine disorders may be accompanied by *rapid heart, the most frequent such cause being* hyperthyroidism

Valvular defects, pericardial lesions, and *high or low blood pressure* may be accompanied by sinus tachycardia, because they either increase the work of the heart and, *therefore, are the equivalent of exertion,* or cause reflex acceleration of the heart beat through changes of stretch of vascular receptors

If the *myocardium is weak,* the heart maintains its output by reducing systolic discharge and *increasing its rate.*

Sympathetic irritation or a lesion of the vagus nerve may be responsible for a rapid pulse.

Signs and Symptoms. The patient usually does not feel the tachycardia, but if it is too high, he may complain of *palpitation*

The *pulse* is regular and often small. It has no fixed rate; therefore, exercise, change of position, and respiration may vary it Spontaneous variations are also common. The *heart sounds* are regular and frequently have equal duration and loudness.

Graphic Methods. ELECTROCARDIOGRAM The atrial and ventricular waves follow each other in a normal way (Fig. 11-1A). The P-R interval may be slightly longer than normal but is not over 0.20 sec. Diastole is short, so that *the end of the T wave is near the following P* wave In the adult, the rate varies between 90 and 150 but is seldom above 100 Occasionally, higher figures have been described.

JUGULAR TRACING There may be fusion of the *V* wave with the following *A* wave.

PHONOCARDIOGRAM The heart sounds are short and loud A triple rhythm is not unusual because of tumultuous ventricular filling.

Diagnosis. Sinus tachycardia can usually be recognized because (1) it is connected with a definite cause; (2) it does not start suddenly; (3) it is well tolerated; (4) very seldom does the rate exceed 150; (5) the rate frequently changes; and (6) there is a normal electrocardiogram.

cardiac muscle and on the vagus nerves) is involved. This is also true for digitalis.

A paralysis of the accelerator nerve is possible in some cases, as a result of a central or peripheral lesion, but this is the least frequent mechanism.

Signs and Symptoms. Symptoms are usually absent, but a further strong stimulation of the vagus (sudden immersion in cold water, emotion, or pain) may cause *fainting* In such a case, a vascular collapse is frequently associated with the bradycardia

The *pulse* is slow and regular but may present marked respiratory arrhythmia. The heart sounds and the pulsations of the jugular veins are normal

The *systolic blood pressure* may be normal or slightly low and is usually accompanied by a large pulse pressure

Graphic Methods. ELECTROCARDIOGRAM. The electrocardiogram is normal and shows a long diastole The P-R interval is normal. The rate is usually between 65 and 50, and only exceptionally between 50 and 40 (Fig. 11-1B)

PHARMACOLOGIC AND FUNCTIONAL TESTS The most important is the *atropine test* Injection of 1 mg atropine sulfate hinders the action of the vagus nerve and accelerates the heart rate Another pharmacologic test involves the *inhalation of amyl nitrite* This is particularly effective in patients with coronary heart disease and bradycardia caused by functional depression of the SA node

Changes of position, exertion, and deep respiration are usually sufficient to accelerate the pulse in persons with sinus bradycardia Compression of the carotid sinus may arrest the heart in patients with bradycardia due to hypersensitive carotid receptors Both this maneuver and compression of the eyeballs may also arrest the heart in patients with an excitable vagus nerve

Diagnosis. Diagnosis is not difficult in most of the cases Clinical data are usually sufficient and may be supplemented by the functional and pharmacologic tests The electrocardiogram may be needed in doubtful cases or when the rate is very slow.

Differential diagnosis should be made from *nodal rhythm, type 2.1 AV* or *SA block*, and *complete AV block* In the latter, there is usually a slower pulse, but patients with congenital AV block may have a pulse between 40 and 60.

Treatment. No treatment is required in most cases. If possible, the cause of the bradycardia should be removed.

In some cases, *atropine, ephedrine, Benzedrine, caffeine*, or *nitrites* will be required. Nitrites are useful only in patients with coronary heart disease

SINUS ARRHYTHMIA

Cause. This common irregularity of the pulse is usually associated with respiration. It is particularly evident in children, convalescents, or persons with unusually high excitability of the vagus nerve. It is also frequently present when pleuropericardial adhesions are stretched by respiratory movements. It may occur in old people with arteriosclerotic lesions and coronary heart disease, and in children with rheumatic carditis.

Signs. The pulse is periodically and alternately rapid and slow Slowing down of the pulse may be abrupt but is usually gradual in onset. The pulse may seem intermittent in the first case These changes of the heart rate are connected with respiration, the phase of rapid pulse occurring in the second half of inspiration and that of slow pulse in the second half of expiration

Deep breathing accentuates the phenomenon, *suspension of respiration* causes its disappearance. *Atropine* usually abolishes sinus arrhythmia

Graphic Tracings. ELECTROCARDIOGRAM. The electrocardiogram has normal waves, it shows, in general, gradual changes in the length of diastole (Fig. 11-1C). If there are sudden changes and the long diastole is equal to twice the P-P interval, the cause is SA block.

ARTERIAL TRACING The pulse waves become gradually larger and have a lower starting point, then become smaller again, with a higher starting point. This indicates higher systolic and lower diastolic pressures during the phase of slower pulse, usually during the second half of expiration

Mechanism. The various mechanisms of sinus arrhythmia are illustrated by the following scheme.

SINUS ARRHYTHMIA

Vagal	Myocardial
Respiratory	Incomplete SA block
Hypoxic (bulbar)	Type I (periodic)
Independent	Type II (intermittent)
	SA standstill

2

Paroxysmal tachycardia

MAX HOLZMANN

Paroxysmal tachycardia is the name given to paroxysmal episodes of rapid heart action with sudden beginning and sudden end. Thus, the term is used in both a general and a limited sense, depending upon whether acute episodes of atrial fibrillation and flutter are included or not. The classification below gives an over-all picture of the various groups as revealed by the electrocardiograph.

HISTORICAL INTRODUCTION

According to Willius and Dry, Williams (1835) first described a case of paroxysmal tachycardia. Payne-Cotton (1867) published a typical case observation. A penetrating analysis of the disease was given by Bristowe (1888), and Bouveret (1889) separated out the paroxysmal rhythmic types from the numerous other forms of tachycardia, and coined the term used at present. Finally, Hoffmann (1900) published a well-known monograph on this syndrome.

With the help of the electrocardiogram, it was possible to separate paroxysmal tachycardia from paroxysmal atrial fibrillation or flutter. The discovery of the ventricular tachycardias was due to the use of the electrocardiograph. As a result, T. Lewis (1909) was able to describe short episodes of ventricular tachycardia in a patient and to produce ventricular tachycardia in a dog by means of coronary artery ligation. Robinson and Hermann (1921) demonstrated that, in man also, ventricular tachycardia can be caused by occlusion of a coronary artery.

DIFFERENTIATION OF THE PAROXYSMAL TACHYCARDIAS

The classification of the entire entity is based partly on clinical findings and partly on the electrocardiographic picture.

CLASSIFICATION OF PAROXYSMAL TACHYCARDIAS

- Paroxysmal tachycardia *in a strict sense*.
  - Essential paroxysmal tachycardia (Bouveret-Hoffmann type).
    - Supraventricular:
      - *Rapid*
        - With } AV block
        - *Without* } AV block
      - Moderate
    - *Ventricular*
      - Rapid
      - *Moderate*
  - Extrasystolic paroxysmal tachycardia (Gallavardin type)
    - Supraventricular
    - Ventricular
- Paroxysmal atrial flutter
- Paroxysmal atrial fibrillation

Clinically, the classical form of paroxysmal tachycardia is revealed by the sudden occurrence of a regular and rapid heart action at 150 to 220 beats per minute (occasionally higher rates were encountered). In adults, the rate is usually below 200, while in infants and small children, it can exceed 300. In addition to the *rapid form of paroxysmal tachycardia,* a less common, *moderate form* can be observed, with a rate of 120 to 135 per minute. The uncomplicated cases are generally typical on account of the remarkable regularity of the rhythm. Two different entities can be separated clinically but without sharp differentiation:

1. The classical *paroxysmal tachycardia (Bouveret-Hoffmann type).* It is characterized by the sudden and unexpected onset of a regular tachycardia and by an equally sudden ending, while between attacks, the heart action is slow and regular or presents, at most, occasional premature beats.

Paroxysmal tachycardia gives an abnormal electrocardiogram, starts suddenly, and is less well tolerated.

Treatment. Treatment is directed, whenever possible, to removal of the cause. Whenever high excitability of the sympathetic system is involved, *ergotamine* or *Hydergine* may be used.

Digitalis or *quinidine* is indicated in some cases. *Coramine* may be used with low blood pressure.

Rest, sedatives, and treatment of the thyroid condition are necessary in some cases. In particularly severe and intractable cases, removal of the upper thoracic sympathetic ganglia (second to fifth) may be necessary.

SINUS BRADYCARDIA

Cause and Mechanism. Sinus bradycardia may result from *poisoning* or *infection*. Poisoning from biliary salts (jaundice) or products of metabolism (uremia) is not uncommon. Poisonous mushrooms, morphine, and digitalis cause bradycardia. Typhoid, diphtheria, rheumatic disease, mumps, pneumonia, and cholera may cause relative or absolute sinus bradycardia. In particular, rheumatic carditis causes bradycardia in about 10 per cent of the cases.

Convalescence is frequently accompanied by a slow pulse due to sinus bradycardia.

Increased intracranial pressure is revealed by a slow pulse *Visceral colicky pain* also is usually accompanied by slow pulse.

Patients with *myocardial fibrosis* may have a persistently slow pulse which is only slightly affected by the position of the patient.

Hypothyroidism is frequently associated with bradycardia, which may even reach the low rate of 40 per minute.

Patients with *abnormal sensitivity of the carotid sinus* have a sudden slowing of the pulse when a change of position or an external compression stimulates the carotid receptors.

Lastly, some *normal individuals* have a constantly slow pulse, their condition has been called *vagotonia*. *Athletes* frequently have a slow pulse.

In all these cases, three possible mechanisms may exist. (1) a continuous reflex action slows down the heart by way of the vagus nerve, (2) there is a high tonus and excitability of the medullary center of the vagus, so that normal stimuli are sufficient for maintaining the slow pulse; (3) the SA node itself is affected.

The reflex mechanism is involved in the cases with visceral pain or hypersensitive carotid sinus and may be involved in cases of myocarditis. A high excitability of the vagus occurs in patients with high intracranial pressure, in hypothyroidism, in drug action, and in normal individuals with slow pulse. Direct change of the function of the SA node is involved in myocardial fibrosis, in severe myocarditis, and also in cases of poisoning. However, in many cases, a double mechanism (action on the

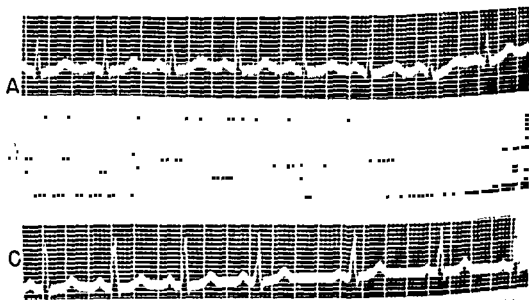


Fig. 11-1. Modifications of the heart rate and rhythm due to the SA node and revealed by the ECG. A. Sinus tachycardia. B. Sinus bradycardia. C. Sinus arrhythmia.

ble that they are also instigated in a similar fashion. In general, there seems to be a great variety of favoring elements. Physical exertion, certain body positions, gastrointestinal distention, constipation, pain in remote parts of the body, or emotion are the most common triggers. A relationship to body position is occasionally demonstrated. In an unusual case described by Fine and Miller, atrial tachycardia began while the patient was in the erect position, had a higher rate while he was standing, a more moderate one while he was sitting, and was even less rapid when the patient was lying down, until it finally disappeared

SYMPTOMS. The onset of the tachycardia is often recognized by the patient through an awareness of the heart Most patients feel a slight *pressure* on the chest, often a slight [illegible] *dyspnea* If cardiac dynamics are [illegible]

[illegible] sations become powerful On the other hand, the rapid rate can be completely unknown to the patient The author discovered paroxysmal tachycardia at a rate of 200 in an ambulatory patient with aortic insufficiency, the patient had no idea of its presence Wenckebach and Winterberg reported a case of a woman who consulted her physician only because she was disturbed, while in company, by visible pulsations of her neck vessels

The rapid heart activity can be felt as palpitation of the precordium or as pulsations in the neck or head. Nausea, sweating, tinnitus, and faintness may occur The attack may be associated with an urge to urinate Less frequently, palpitation is associated *with precordial pain* If it is of slight degree, the latter is not alarming However, if it is severe, the presence of coronary sclerosis must be considered Sometimes, there is a "status anginosus," which *persists* as long as the tachycardia. Under these conditions, the persistence of precordial pain, even for several hours, *should* not be accepted as evidence of an infarct If the pain still persists *after* the termination of the tachycardia, on the other hand, an infarct has probably occurred Occasionally, the end of the attack is *particularly* unpleasant. A *lightning-like pain* in the *cardiac region,* often with radiation to the left arm, or *vertigo, or even loss of consciousness* may terminate the attack. The latter may be due to *cardiac arrest* lasting several seconds. Most often the patients cannot describe the end of the attack because it is followed by sinus tachycardia. After the attack, many patients feel tired and weak for hours; others, on the contrary, are immediately able to resume their activities.

OBJECTIVE FINDINGS During an attack of tachycardia, the examining physician should count the rate during auscultation of the heart, because the pulse count is often misleading. The *radial pulse* may be small and weak, may vary in fullness with respiration, may alternate, and may be uncountable or even imperceptible. Occasionally, *pulsus alternans* can be demonstrated by a sphygmomanometer (or a pulse tracing) even though palpation fails to reveal it.

Often, strong pulsations of the *jugular veins* are present. Wenckebach (1910) first recognized this phenomenon in the phlebogram and stated that it was caused by summation waves due to superposition of the A and C waves of the venous pulse. If the attack ended, the pulsations also disappeared. *Auscultation* of the heart is characterized by a similar duration of the interval between the two heart sounds, designated by Huchard as *embryocardia* In other cases, the 1st heart sound is much louder than the 2d, in fact, the latter may be imperceptible Then, the danger of counting only one-half the beats must be avoided Previously existing *murmurs may* disappear during the tachycardia, or a *rough systolic murmur* may be added. A final evaluation of the auscultatory findings of the heart, and the conclusions drawn from them, must *therefore* be delayed until the attack is over.

The evaluation of *heart size* is today based on *x-ray* findings, *which* can be interpreted correctly only through comparison with films taken between attacks In uncomplicated cases, it can be demonstrated that the heart becomes *smaller* during the attack, which is what one would basically expect since diastole is relatively more shortened than systole (Dietlen; Groedel, Vaquez and Bordet). This is especially noticeable during a prolonged attack, and then atrial dilatation occurs as a result of venous engorgement and ineffective atrial contractions, a fact which is particularly true *for the* right atrium. After termination of the attack, a return of the right atrium to normal size can be *noted*, although the size of the

Diagnosis. The diagnosis can be made by means of the simple tests already described. Suspension of respiration causes a disappearance of the phenomenon. Atropine can be used in doubtful cases.

Differential diagnosis should be made with SA block. *Periodic SA block* may be connected with respiration and may be affected in the manner of respiratory arrhythmia by the functional tests. However, in SA block, *the long pause is equal to twice the short one;* in respiratory arrhythmia, the long pause is *less than double;* the increase is gradual in the latter.

Prognosis and Treatment. Prognosis is favorable except in those cases where the irregularity reveals an initial cardiac failure (coronary heart disease or acute rheumatic carditis. Therefore, correlation between sinus arrhythmia and all other clinical data is necessary.

No treatment is necessary. Atropine may cause disappearance of the disturbance.

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lepsy were not established either during an attack or in the intervals.

The Electrocardiogram. The ECG is, as a rule, characterized by the regular succession of ventricular complexes of supraventricular origin, usually with normal QRS duration and of normal pattern, at a rate of 150 to 220 in the typical form, and of 120 to 150 in the moderate type. *The atrial waves have the same rate as the ventricular and have a constant relationship to the latter.* The configuration of the P waves is variable according to the origin in higher or lower parts of the atrium, as in atrial premature contractions (Fig. 11-2). In general, the P waves reveal that the stimulus is conducted in an upward direction. When no P waves are visible, they may be buried in the QRS complex or in the T wave of the preceding cycle. When the P wave is hidden by the QRS interval because of simultaneous activation of the atria and ventricles, there is an AV (nodal) origin of the stimulus. When the P wave is hidden in the T wave, there usually is delayed stimulation of the atria. These situations, as well as the difficulty of differentiating whether a negative P wave belongs to the preceding or the following cycle, have led to the adoption of the general term of "supraventricular tachycardia" instead of "atrial" or "nodal tachycardia." A differentiation often can be made only when one can observe the onset of an attack. If this begins with a ventricular complex followed by a negative P wave in lead II or III, or without any P wave, there is a nodal pacemaker.

In the form of extrasystolic paroxysmal tachycardia, the relationship of the atrial and ventricular complexes is basically the same. At the termination of the attack, *premature contractions* often occur. They have the same pattern as the complexes of the tachycardia. It is impossible to draw a sharp line of division between a premature contraction with repetitive formation and an extrasystolic tachycardia. In general, a run of more than 6 to 10 extrasystoles is called extrasystolic tachycardia.

The relationship between P waves and ventricular complexes is similar to that found in atrial, nodal, and ventricular extrasystoles. The *ventricular complexes* differ more or less from those of the normal sinus rhythm because of slight flattening of the T wave and depression of the S-T segment. Not infrequently, however, a significant S-T depression is noted and should be interpreted as the result of a *relative coronary insufficiency.* As this occurs also in young and healthy patients, it is not indicative of coronary artery disease. While precordial pain can be completely absent, a *typical ischemic pain* can be induced by the tachycardia in patients with coronary arteriosclerosis.

Occasionally, the ventricular complexes show an *alternating pattern* which usually involves both the form and the amplitude of the QRS complex.

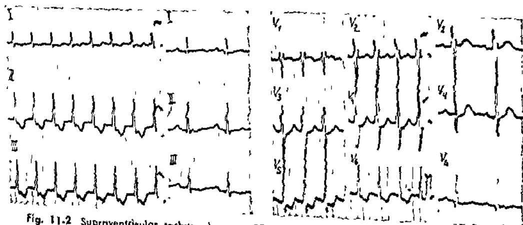


Fig. 11-2 Supraventricular tachycardia in a 37-year-old man without other abnormal cardiac findings. A. After a 3-hr attack with a heart rate of 180. The position of the P waves can be established in lead V_1. B. After an intravenous injection of 1.0 cm³ of Mestinon and carotid sinus pressure, there is sinus rhythm at a rate of 95. Reflex slowing of the heart had been unsuccessfully tried prior to the injection.

2. *Paroxysmal extrasystolic tachycardia (Gallavardin type)*. Runs of tachycardia follow each other for various periods of time, while in the intervals, there are single or short series of extrasystoles. In this way, palpation of the pulse may give the impression of an arrhythmia Among the subgroups described by Gallavardin, three deserve special mention:

a *The excitable form of paroxysmal tachycardia ("tachycardie à centre excitable")*, in which the attacks are not completely without cause and are easily provoked by slight physical strain or psychic excitement Sometimes, as a result, there are extremely numerous attacks, most of them brief However, the heart does not return to a normal rhythm in the intervals because of the frequent premature beats. The extraordinary lability of this condition constitutes a serious drawback for the patient.

b. *The prolonged form of extrasystolic paroxysmal tachycardia ("extrasystolie à paroxysmes tachycardiques")* or "repetitive paroxysmal tachycardia" of Parkinson and Papp, which is distinguished by its persistence over long periods of time (even many years) with only short interruptions of extrasystoles. This form has no apparent cause.

c. *The terminal extrasystolic tachycardia* occurs in patients with advanced coronary insufficiency and represents a prefibrillatory stage of severe prognosis

The *ECG* makes it possible to divide the various forms of paroxysmal tachycardia *according to their origin* into *supraventricular* and *ventricular* It also permits one to evaluate irregularities of rhythm, if they occur This differentiation is of particular interest for therapy.

The pulse rate permits a presumptive differential diagnosis, but whenever possible, it should be confirmed by electrocardiography The distinguishing features of the various types can be described as follows.

In *essential paroxysmal tachycardia (Bouveret-Hoffmann type)*, the attack may last from a few seconds to several days It is followed by completely normal rhythm. During the attack, there is a regular rhythm with a rate of from 120 to 220 beats per minute in adults, and often over 300 in small children. The typical attack of palpitation usually is in the range of 165 to 200 in the adult

In *extrasystolic tachycardia (Gallavardin type)*, there are occasional short runs of extrasystoles, and the attacks can follow each other with short pauses for a long period of time. The rate is somewhat lower, ranging from 125 to 190, and the rhythm is often not so regular as in the previous type.

The ventricular form of tachycardia may be transformed into dangerous attacks of *ventricular flutter* (regular rate over 300) or *ventricular fibrillation* (irregular rhythm).

The regular forms of atrial flutter are associated with a much more narrowly limited ventricular rate, which with a 1:1 conduction lies at 195 to 220, and with a 2:1 conduction, at 130 to 150. Therefore, a differentiation is often possible.

The *frequency range of the tachyarrhythmias* is in contrast very large, and stretches from an upper limit of about 215 down to the normal range, in which it loses its paroxysmal aspects. This range is determined mainly by the variable AV conduction in *atrial fibrillation, atrial flutter*, and *extrasystolic tachycardia*

SUPRAVENTRICULAR TACHYCARDIA

Under this designation are grouped all paroxysmal types which have their origin in the region of the atrium or in the AV node. These, in turn, should be divided into *sinus, atrial*, and *nodal* tachycardia. The occurrence of paroxysmal sinus tachycardia has not been demonstrated. According to the view of most of the current authors (Scherf and Schott, 1953, Bellet, and others), nodal (AV) tachycardia is rare. *Supraventricular tachycardia is usually caused by an atrial ectopic focus*. For this reason, these forms are often grouped together under the name of "atrial" tachycardia. The term chosen here, however, is preferable because it includes all the possible forms

The Clinical Picture. In general, the patient with a typical form of paroxysmal tachycardia experiences an attack in a completely unexpected manner He is usually in a normal state of health and may be asleep. Exceptionally there is a *premonitory warning*, usually a general feeling of malaise hours or days before

plexes often show some inversion of the T waves in various leads for several days or even weeks (*posttachycardial syndrome*).

Occurrence. Supraventricular paroxysmal tachycardia occurs at any age, however, it is relatively rare in newborn infants and young children There is no sex difference. Cases of familial occurrence have been reported.

The frequency of supraventricular paroxysmal tachycardia is difficult to determine, since some patients have never been checked during an attack, and others probably never realize that they are having an attack and therefore never report it

Kissane et al. analyzed the heart findings and clinical condition of 361 patients with supraventricular tachycardia, presenting the following data.

Percentage	*Finding*
34	No other illness demonstrable
34	Rheumatic heart disease
14	Arteriosclerotic heart disease
3	Hypertensive heart disease
5	Thyrotoxicosis
10	Other findings

The authors then compared these percentages with those of all the patients in their practice having these diseases From this, they realized that these attacks occur much more frequently in rheumatic than in arteriosclerotic heart disease, and that hyper- and hypothyroidism have no influence

The general experience is that, in at least one-third of the cases, the heart is normal

Mechanism. In order to explain paroxysmal tachycardia, we must consider the fact that the stimuli of either supraventricular or ventricular origin arranged in rapid sequence can occur with the same coupling as with individual extrasystoles No sharp distinctions can be drawn between runs of extrasystoles in series and paroxysmal tachycardia Therefore, premature contractions and paroxysmal tachycardia must have a similar mechanism

The theory of a *circus movement* was advocated by Mines Lewis refused to accept it in paroxysmal tachycardia His reasons were that it was not proved that extrasystoles were due to a circus movement, that the rate is lower than in flutter, that the stimuli were not necessarily arranged in series, and that no sufficiently long pathway was available in the atria to permit a circus movement at the necessary speed De Boer invoked the existence of the *bundle of Paladino-Kent* in order to explain supraventricular tachycardia. The stimulus would run upwards through the bundle of His and then over the accessory bundle back to the atrium, or in the opposite direction While this could be admitted in the Wolff-Parkinson-White syndrome, the explanation certainly is not valid for the other forms.

Ashman and Hull resorted again to the "circus" theory by admitting a *functional*, longitudinal dissociation in the bundle of His permitting both an atrial and a nodal pacemaker (in cases with retrograde conduction, possibly even a ventricular). A premature atrial beat would stimulate only part of the conduction system while the rest would still be in a refractory state. From the first group of fibers, the stimulus would be transmitted to the second and, through it, back to the atrium, which would again be stimulated.

The *theory of frequent heterotopic impulse formation* has more supporters today than the circus theory Scherf (1928, 1948, 1953), as well as Prinzmetal (1950, 1952), and their coworkers, have advocated this theory. The following points are presented in its favor:

1 In animal experiments, local application of barium chloride, digitalis, or strophanthin causes the formation of an extrasystolic focus. Warming of this focus is followed by paroxysmal tachycardia, which continues as long as the warmth is maintained (Scherf, 1948).

2. A circus movement within the atria is excluded because of the relationship between period length and speed of spread on the one hand, and length of the available path on the other (Lewis, 1925)

3 Sudden doubling or halving of the atrial rate (from 107 to 214—Camp and Scherf; a few observations from 90 to 180 and back) with unchanged P waves is compatible with a 2.1 exit block of the ectopic impulse.

4 The occurrence of an interference dissociation cannot be explained by a circus movement but is easy to explain by ectopic impulse formation (Schott, 1946)

Prinzmetal et al. (1950) provoked atrial tachycardia in the dog by means of chemical, electrical, and mechanical stimuli, and registered it on ECG moving pictures, and with the oscilloscope In all records, they found a spread of the impulse occurring in all directions. When they stimulated mechanically the atria of patients undergoing chest surgery,

rest of the heart increases. In paroxysmal tachycardia of long duration (or with a damaged myocardium), a *globular cardiac enlargement* can be observed. This indicates that the contractile strength of the ventricles is poor, so that the *diastolic residual blood is increased* even in the ventricles. After the attack, the dilatation of the heart regresses.

The enlargement of the heart is often associated with a *widening of the large veins* due to engorgement, particularly apparent in the region of the superior vena cava.

The stroke volume is greatly decreased in paroxysmal tachycardia. Barcroft et al., in two cases having a rate of over 200, found the stroke volume decreased from 77.5 to 12.9 cm^3, and the cardiac output from 5 to 6 liters to 2.1 to 2.8 liters/min. The elevated heart rate therefore cannot compensate for the decreased stroke volume, and the output is diminished to one-half or one-third of normal. The decrease of stroke volume can be explained by *the inadequate filling of the ventricles*. While at a rate of 50, diastole lasts twice as long as systole, at a rate of 150, it lasts only one-half as long as systole. With further increase of heart rate, as a result of the relationship between heart rate and length of diastole, theoretically a crit'cal rate could be *attained, in which the entire cycle would* be occupied by systole. According to Bazett's and Hegglin-Holzmann *formulas*, this rate would lie between 260 and 370. Other factors render the attainment of such rates impossible in adults. The heart size plays a certain role because small human hearts with a high resting rate can *tolerate remarkably well further* increases in rate, while large hearts with a slow basal rate withstand relatively poorly lesser increases. Under otherwise normal conditions, the maximum tolerable rate is about three times the resting rate of a heart (v. Boros).

BLOOD PRESSURE Usually there is a moderate drop of systolic pressure and no change of the diastolic pressure. This can be explained by the frequency of small pulse waves, obviously connected with short intervals, during which less of a diastolic drop is possible. The *coronary flow* is adversely affected by the paroxysmal tachycardia because the duration of diastole, during which a large part of flow takes place, becomes especially brief. The lowered aortic pressure is a further cause of deterioration.

Wégria and Keating induced paroxysmal tachycardia in a normal dog and observed a temporary backflow in the coronary vessels *and a drop of the mean pressure.* In moderately rapid tachycardias, both returned in a short time to the initial values or (uncommonly) even exceeded them. With very high rates, however, they remained low for the duration of the attack. The rates being equal, coronary flow and mean pressure are more severely decreased in ventricular than in supraventricular tachycardia. After termination of the tachycardia, mean pressure rises first and may become higher than normal.

Peripheral circulation is usually poor. Patients are pale and their extremities are cool. If there is concomitant heart disease and the attack is prolonged, *cyanosis and venous engorgement* are common.

Poor systemic circulation is followed by inadequate oxygenation of the blood and may be revealed dramatically by *Cheyne-Stokes respiration.* This disturbance may occur early in patients having heart failure, or, if there is no heart disease, it may be provoked only by episodes lasting several days.

A characteristic phenomenon is a *sudden, profuse diuresis,* which occurs at the end of an attack. The urine has a light color and a low specific gravity. This urinary flow may also occur in tachycardia associated with atrial fibrillation or flutter.

Blood gas analysis during an attack was made by Carter and Stewart, as well as by *Dieuaide et al.* They observed a moderate decrease of oxygen saturation in the arterial blood and a severe decrease in the venous blood. Accordingly, the arteriovenous oxygen difference was greatly increased.

A relationship between paroxysmal tachycardia and epilepsy was considered long ago. More recently, accurate studies were made with the aid of the EEG (Gérard, Naquet, Gras, and Jouvet). In three EEGs taken during paroxysmal tachycardia, an increase of the rapid waves seemed likely, and there was a tendency to alteration of the alpha waves. Between attacks, whatever the type of tachycardia, nothing could be seen in one-half the cases, and in the other half, there were only slight variations, such as absence of alpha waves. Specific changes similar to those of epi-

is unsuccessful. Bilateral compression of the carotid should not be attempted since it causes cerebral anoxia. Unconsciousness and convul- [illegible] sinus pressure apparently was followed by cerebral thrombosis

If this maneuver is ineffective, *ocular pressure* should be attempted Intense pressure below the supraorbital ridges on the downward turned eyeballs is usually painful and should not be attempted on injured eyes. It causes a powerful *oculocardiac reflex.*

The success of these measures depends upon the skill of the operator and the type of attack. Success is claimed by various authors in from 10 per cent (White) to 80 per cent (Bellet) of cases If one of these methods works and the patient suffers frequent attacks, it is recommended that either he or the people around him be instructed in the use of the maneuver

MEDICATION *Parasympathomimetic drugs* Individual sensitivity to these drugs varies strongly Unpleasant side effects, such as nausea, vomiting, salivation, sweating, hyperpnea, and drop in pressure, can occur For these reasons, the following precautionary rules should be followed when these drugs are to be given by injection

1. The application should always be made with the patient lying down

2 A hypodermic syringe containing 0 5 to 1 0 mg *atropine* as an antidote should be ready for intravenous injection

3 Bronchial asthma and coronary sclerosis are contraindications

As all these drugs sensitize the vagal receptors, reflex vagal stimulation may become successful if tried a few minutes after their administration *Physostigmine,* 0 5 to 1 5 mg subcutaneously, has been used by Kaufmann (1912) (in combination with digitalis) and by de Meyer (in combination with strophanthin)

Prostigmine (*neostigmine*), 0 5 to 1.0 mg subcutaneously or intramuscularly, has proved successful (Waldman and Pelner) Intravenous administration should be avoided because dangerous The oral route is less reliable Abdominal cramps and diarrhea are common side effects.

Mestinon (pyridostigmine bromide), 1.0 to 2 0 mg intramuscularly, or 1 mg intravenously, or 20 mg four times a day orally, has a milder action.

Acetylcholine was recommended by Segers and coworkers (1945) as follows: intravenous injection of 20 mg (1.0 ml of 2 per cent solution), if this is without effect, the injection is repeated every 3 to 4 min with increasing doses of 40, 80, and 100 mg, as necessary. The effect usually occurs within 30 sec. Because a significant drop in blood pressure can occur, the patient should be supine and a syringe containing 0 5 to 1.0 mg atropine should be available.

Doryl (Merck) (carbaminol-choline-chloride) has been recommended similarly for intravenous injections (Birk, Lethaus, and Plugge). If ½ ampule (0 25 mg in 1 ml) is not sufficient, it can be repeated after a short time. The injection must be given very slowly in order not to cause a prolonged cardiac arrest.

Acetyl-beta-methylcholine (*Mecholyl*) was recommended by Starr (1933, 1936) and by Morgan in subcutaneous doses of 10 to 50 mg (average 25 mg). It is claimed that it terminates 90 per cent of the attacks. It should *not* be given intravenously. Its action becomes manifest within a few minutes. Side effects are more frequent and more severe than with acetylcholine, and even fatalities have occurred. With the transition to sinus rhythm, a short ventricular tachycardia of the fibrillatory type can occur (Bellet).

Strophanthin may terminate an attack immediately after one intravenous injection of 0 75 mg (Volhard), or one to two injections of 0 5 mg or three to four injections of 0.3 mg (Edens and Weese). Possible dangers of such large doses should be considered, especially if there has been previous digitalization or if the patient has coronary sclerosis.

Digitalis preparations are preferred today in the treatment of supraventricular paroxysmal tachycardia (Wilson and Wishart; Bohnenkamp). Intravenous injection of 0 8 to 1 6 mg *Cedilanid* can result in a sudden interruption of the attack (Kroetz) or in its arrest within 20 min (Weissberger and Feil). A similar effect can be obtained with *digitoxin* or *acetyldigitoxin* (*Acylanid*) in dose of 1 3 to 2 0 mg in one to two intravenous injections (Spang, Loeffler et al).

In rare cases, the ventricular action may be irregular or slow, thus rendering the diagnosis particularly difficult. However the ECG will give the clue and solve the problem. The findings are.

1. *Irregularity of a supraventricular rhythm.* This is possibly connected with a variation of the P wave; it is usually the result of an extrasystolic type and is of moderate rate.

2. *AV conduction disturbances.* With changing rates, the conduction time can be slightly variable. If there is a 2° *AV block* with occasional dropping of stimuli, the picture of a tachyarrhythmia will take place. Poor AV conduction due to ischemia, infection, or digitalis glycosides predisposes to this picture. When there is a 3:1 or 4:1 type of block, the tracing may simulate that of atrial flutter. Finally, in complete AV block, the ventricular action is regular and slow.

3. *Addition of ventricular extrasystoles.* This occurs usually only at moderate rates, because otherwise the coupling is longer than the diastolic interval. There may be a combination of stimuli, so that ventricular activation is due partly to an extrasystolic focus and partly to a stimulus carried by the bundle of His. A rare occurrence is the combination of supraventricular and ventricular tachycardia

4. *Alternation* in the duration of AV interval is rare (10 out of 100 cases, Barker, P S, et al, 1943).

Complicated ECG findings can make the diagnosis of supraventricular paroxysmal tachycardia more difficult They may be the following.

1 *The patient already has a bundle branch block* This may give the impression of a ventricular tachycardia The problem is clarified only by the examination of previous or subsequent tracings Moreover, there are no P waves with a slower rate than the ventricular

2 *Intraventricular conduction disturbances* Strain of the ventricular conduction may cause variations of the intraventricular conduction, at times simulating the picture of bundle branch block It is important to note the constant relationship between the atrial and ventricular complexes The beginning of an attack is revealed by a premature P wave.

3 *Nodal tachycardia with interference dissociation* In a nodal tachycardia with retrograde block, it is possible that, occasionally, a P wave originating in the SA node finds the AV conduction system and the ventricles not in a refractory phase, thus resulting in a conducted beat. Since such ventricular complexes occur somewhat prematurely, they cause a slight arrhythmia. This sequence can be expected only *in* the type with moderate rate because of the longer refractory period of the ventricle (Schott, 1946).

Interpretation of the ECG can be clarified, at least in some cases, by *special observations* during and between attacks.

1. Observation, if possible, of the *beginning* or *end* of the attack, a feat which is less difficult in extrasystolic tachycardia than in the other types.

2. Depression of the rate or change of the conduction time, by means of *carotid sinus pressure,* so that the relationship of atrial and ventricular complex changes and P waves may be revealed. Blocking the AV conduction may reveal atrial flutter with rapid ventricular action. In atrial tachycardia, the P waves may appear, or the attack may be terminated.

3. The use of special ECG leads, particularly the *esophageal leads,* can reveal the P waves.

The *transition from paroxysmal tachycardia to sinus rhythm* (either spontaneously or following vagal stimulation) can occur in the following ways (Hellerstein and coworkers):

1. *A posttachycardic pause,* lasting several seconds and followed by sinus rhythm, is common

2 *The rate may become slower,* then suddenly change to a sinus rhythm

3 The transition can be *gradual.*

4. There is first a slowing, then a pause, and then the onset of sinus rhythm.

5 In the posttachycardic phase, one or more *nodal escapes* occur, then a few ventricular premature beats, possibly polifocal, until sinus rhythm is reestablished.

Prolongation of the AV conduction and *aberrant ventricular response* can also occur.

The manner of termination of the attack is not always the same, even in the same patient. If during the tachycardia, there is a significant S-T depression, it usually disappears rather quickly However, if the sinus rate is still relatively high after the end of the attack, the depression lasts for a longer time After attacks lasting for several days, the ventricular com-

VENTRICULAR TACHYCARDIA

The Clinical Picture. In contrast to the supraventricular form, these attacks, as a rule, occur in individuals having cardiac disease They are, therefore, only part of the clinical picture, may be unrecognized by the patient, and often are not properly evaluated by the physician, at least in a first period.

The duration of the attack may vary. Most episodes last from a few seconds to several days Attacks lasting from 3 to 4 weeks are not unusual The longest ventricular tachycardia, lasting 77 days, was described by Mays

If an episode of ventricular tachycardia has occurred once, there is a tendency for its repetition These attacks can occur either after brief intervals or, on the contrary, only after several years They may tend to become more frequent with time On the other hand, there may be a single episode—e g , after a coronary occlusion, followed by permanent recovery or. at times, having a fatal outcome

Symptoms and Signs They vary considerably according to the underlying heart disease and the duration of the attack If there has been heart failure, ventricular tachycardia may be completely unapparent and masked by the general picture If the attack lasts for several days, increasing signs of circulatory insufficiency, such as *dyspnea, somnolence*, and *pain in the right hypochondrium*, often occur If the attack follows an infarct, either a *status anginosus* (persistent precordial pain) or a sudden *collapse* may be the consequence

Occasionally, certain clinical *signs* indicate the nature of the tachycardia They are not always present, however, and at times may be doubtful, so that the final diagnosis is always made through the ECG.

The ventricular rate can be determined by simultaneous auscultation of the heart and palpation of the pulse It is usually between 160 and 180, but it may be as low as 125, particularly under the influence of medication On the other hand, if ventricular flutter occurs, the rate may exceed 200

The cardiac rhythm may be completely regular Several authors (particularly Strong and Levine, S A , 1927) emphasize that ventricular tachycardia is less stable than the supraventricular However, they *most* likely refer to cases of extrasystolic tachycardia with short pauses, during which single extrasystoles occur. In these cases, one has the impression of a considerable arrhythmia, even simulating that of atrial fibrillation.

On auscultation, *the heart sounds show different degrees of loudness* if the atria are still ruled by a SA pacemaker. Levine (1921) showed that the 1st heart sound presents periodical changes of intensity. As in complete AV block, the 1st heart sound is louder (*cannon sound*) if the atrial and ventricular contractions occur at the same time or if the atria contract 0 05 to 0.12 sec before the ventricles (Duchosal). Obviously, this phenomenon does not occur if there is atrial fibrillation or retrograde atrial stimulation Apart from these cases, periodic intensification of the 1st sound is demonstrable in about 50 per cent of the cases (Armbrust and Levine).

Another phenomenon occasionally determined at auscultation may be *misleading: only* the 1st sound may be heard, or even more misleading, its loudness may alternate (Armbrust and Levine) Then, it is possible that only one-half of the ventricular beats are counted. The peripheral pulse can *sometimes* clarify the situation, the ECG always does so.

The *arterial pulse* is mostly small and often difficult to palpate Occasionally, it shows a *periodic intensification* If *one* can exclude any connection with *respiration*, such a finding is typical of ventricular tachycardia. The larger pulse waves occur when an atrial contraction falls at the end of a *ventricular systole* or with a short ventricular diastole, while the pulse is small or *absent* if the onset of the atrial contraction occurs at the beginning of a ventricular *systole* (Fischer; Lian et al., 1931; Zeh) When an atrial contraction occurs simultaneously with a ventricular, it forces the blood backwards *into* the large veins and there is less venous return shortly thereafter, so that the subsequent ventricular filling is decreased. In cases with dissociation, the arterial pulsations were recorded graphically and found to be decreased when the R-P interval was between 0 06 and 0.18 sec.

In the *venous tracing*, a tall wave can be observed at the time of the "cannon sound" (Gallavardin, 1920) Careful *inspection* of the jugular *veins* reveals pulsations *which* occur at about *one-half* the rate of the ventricular systoles as determined by auscultation, and

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ystoles between attacks as during an attack ndicates ventricular tachycardia

The ECG can show other characteristics:

1. *Alternating ventricular complexes can occur.* There may be a *monophasic*, homolateral alternation consisting of changing amplitude of part of the ventricular complex, or a *diphasic*, bilateral alternation consisting of a change of polarity of the ventricular complex and indicating alternative pacemakers in the two ventricles (Fig. 11-4). The latter is encountered especially under the action of digitalis glycosides. The duration of the ventricular complex may be stable or alternate.

2. The ventricular complexes may be *poliform.* Then the ventricular action is generally irregular and, as a rule, is associated with atrial fibrillation (Fig 11-5A). These tachyarrhythmias represent a dangerous condition, which usually is followed by ventricular flut-

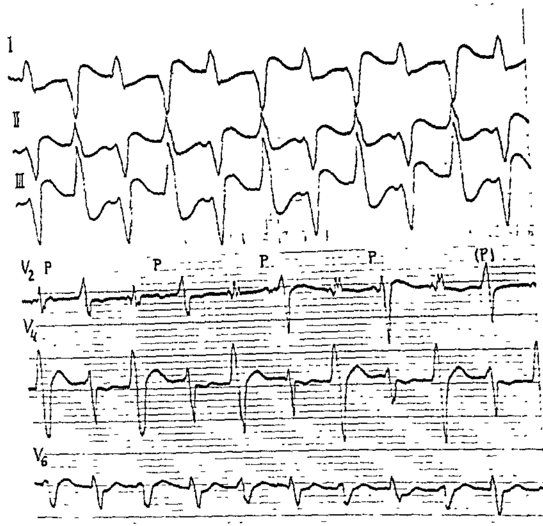


Fig 11-4. Paroxysmal alternating ventricular tachycardia in a 55-year-old man with decompensated hypertension after a 10-day treatment consisting of daily intravenous injections of 0 25 mg Strophosid, 0.25 Gm Euphylline, and 10 ml of 5 per cent glucose. Mean ventricular rate, 143 to 153 The phasic alternation is most marked in the limb leads The independence from a sinus rhythm is demonstrated by the "wandering" P waves in the precordial leads There is at times a definite alternation of the ventricular complexes The ventricular tachycardia disappeared after discontinuation of strophanthin. The patient died 2 months later. At autopsy, severe bilateral hypertrophy with fatty degeneration of the myocardium, a subacute infarct in the left papillary muscle, and renal arteriosclerosis were found.

they repeated the same observations for both extrasystoles and tachycardia.

Pathologic Findings. Occasional deaths of patients with supraventricular tachycardia have revealed gross anatomic findings corresponding to the accompanying disease. In other accidental deaths, these findings have been absent. Precise histologic examinations are rare. Most of the studies have revealed changes in the area of the SA node, the atria (especially the right), the AV node, and the bundle of His.

Mackenzie (1908) described a case with obliteration of the nutrient artery of the AV system, and a case with fibrotic changes in the SA node. Cade and Rebattu (1911) described a case with round cell infiltration and connective tissue hyperplasia in the bundle of His. Butterfield and Hunt studied a case with cell infiltration of the wall of the right atrium, including the SA node. Falconer and Duncan examined the heart of a case with interstitial lymphocyte accumulation in the right atrium, SA node, and AV node area Mahaim (1932) studied a 14-month-old child who had suffered from an uncontrollable supraventricular tachycardia following influenza. In the right atrium, widespread foci of lymphocytes and polymorphonuclear leucocytes, which had involved the SA node region, were found Piotti (1945) studied an 11-month-old child, who had suffered from a sustained supraventricular tachycardia for 7 months, and found interstitial myocarditis (Fiedler type) involving the right atrium and particularly the area of the coronary sinus

Prognosis. The prognosis of the supraventricular tachycardia is usually good Death during an attack is rare However, it may occur in cases with myocarditis or coronary heart disease.

The prognosis should be guarded if a serious heart condition is present, particularly coronary heart disease. If the blood pressure is low, the dangers represented by prolonged or frequent attacks are greater Among other complications, thromboembolic phenomena may occur In these cases, the prognosis is based upon the speed and efficacy of treatment.

In normal hearts, even prolonged and frequent attacks are well tolerated. Noteworthy are the cases in infants and adolescents who may have prolonged extrasystolic tachycardia lasting even 10 years without permanent damage and finally disappearing.

The *life expectancy* is not shortened by paroxysmal tachycardia in an otherwise normal heart. Campbell and Elliot found among 100 cases, 3 who experienced paroxysmal tachycardia for longer than 50 years, and 18 who had it for longer than 20 years. Cooke and White observed a man, still active at 72, who had suffered attacks of paroxysmal tachycardia since the age of 7. It is possible that paroxysmal tachycardia which starts at an older age should be considered more seriously. While Campbell and Elliot admit this point, Cooke and White (1942) find no difference in the prognosis whether the first attack occurred before or after the fortieth year of age.

Treatment. Medical management has two objectives: cessation of the attack and prevention of its repetition.

The treatment of the attack is frequently successful in the supraventricular paroxysmal tachycardia and is based on *reflex stimulation of the vagus nerves.* Often the patient himself has discovered certain means of depressing the attack and the physician can use similar methods. If they do not succeed, he can resort to well-known methods of vagal stimulation If these also fail, certain drugs are available which will either stop the attack or act within a short period of time. In the greatest number of cases, these means are successful; reflex stimulation should always be tried first If one resorts to medication, one should begin with the most harmless.

THE MECHANICAL REFLEX INFLUENCES Certain methods have been shown to be of benefit in individual cases These are curling of the body, lying down with the head below the level of the body, strenuous tensing of the abdominal muscles, the Valsalva or Muller maneuvers, production of nausea by stimulation of the palate, or drinking of iced water. If these measures do not suffice, stronger *reflex vagal stimuli* should be attempted Since before the establishment of a sinus rhythm, a significant "preautomatic" pause can occur, with at times a cardiac arrest of a few seconds, these measures should always be undertaken with the patient lying down.

Carotid sinus pressure is in general the most effective It should be done with constantly increasing intensity while monitoring the heart action and should be discontinued as soon as the tachycardia disappears, so that an unpleasant cardiac arrest will be avoided. First, one should try one side, then the other. Repeated stimulation of the same side generally

ter and fibrillation (*prefibrillatory phase of Gallavardin* or *ventricular anarchy of Clerc and Levy*).

3. If the ventricular stimuli follow each other in rapid sequence, so that their beginning and end can no longer be distinguished, and if, moreover, diphasic undulations occur, then ventricular tachycardia has become *ventricular flutter*.

4. A retrograde conduction to the atria, as a rule, does not occur; however, since no AV block is present, a *pararrhythmia* may arise, causing an *interference dissociation*. As a result of the high ventricular rate, and probably as a result of penetration of impulses into the lowest portion of the conduction system rendering it refractory, there is very seldom an AV conduction If such a conduction exceptionally occurs (particularly when the ventricular rate is moderate), it is revealed by a few premature ventricular complexes without the typical bundle branch block appearance, or by *fusion beats* when the rates are similar, so that the ventricles are stimulated partly through the bundle and partly by an ectopic ventricular focus (Holzmann)

5 In rare cases, a *retrograde conduction of the ventricular impulse to the atria can be observed*, similar to that which may occur in ventricular extrasystoles Then, negative P waves can be seen in leads II and III following the QRS complexes The retrograde mechanism becomes especially clear if the retrograde conduction is combined with a *second-degree retrograde block with Wenckebach periods*. Then, the ventricular complexes continue undisturbed while the negative P waves migrate farther and farther from the QRS complex until one is dropped and the sequence begins again (Fig. 11-6). In the *differential diagnosis* of this form, one should consider supraventricular tachycardia, as well as atrial fibrillation and flutter, with previous bundle branch block, or a functional bundle branch block caused by the tachycardia. Tracings recorded before the attack are, therefore, always extremely helpful.

If there is considerable variability of the ventricular rate, *atrial fibrillation with a functional bundle branch block* should be excluded before admitting a ventricular tachycardia. If atrial fibrillation with conduction to the ventricles was present prior to the attack, the assumption of ventricular tachycardia is justified by the appearance of an independent ventricular stimulation occurring *by attacks*. There are, however, cases of atrial fibrillation with severe variations in the AV conduction and with a threshold value of the *conduction in* the bundle, which causes this to become deficient if the rate is high The more regular and rapid the ventricular rate, the more likely is the assumption of ventricular tachycardia. This may be confirmed by finding ventricular complexes with the same coupling as that of extrasystoles between attacks.

Supraventricular tachycardia with a second-degree AV block can simulate *runs* of ven-

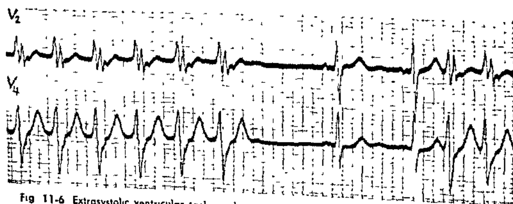


Fig 11-6 Extrasystolic ventricular tachycardia in a *62-year-old* woman, range from 143 to 153. *Retrograde* conduction to the atria with Wenckebach periods The *second* ventricular complex shows no retrograde conduction The RP measured 0.1[illegible]

[illegible] d

[illegible] is 00.

Because the digitalis, in addition to its direct action on the heart, decreases the threshold of the carotid sinus, it is worthwhile to press the carotid sinus again 20 to 30 min after the injection, in case the desired result has not occurred. This should always be tried before further digitalis injections are given. Digitalis therapy is indicated if the tachycardia occurs in a damaged heart or in the presence of congestive failure, and if the reflex vagal stimulation was unsuccessful.

Quinidine acts by depressing all properties of the heart. It should not be used if there is heart failure but can be resorted to in other cases if carotid pressure and digitalis have failed. Quinidine is given orally as *quinidine sulfate* in dose of 0.4 Gm four to six times daily. If the oral route cannot be used or rapid action is necessary, *quinidine gluconate* 0 4 Gm can be given intramuscularly (Bellet) and repeated after 2 hr if necessary. The intravenous approach is not advisable because of possible unpleasant side effects

Magnesium sulfate acts like quinidine; 10 to 20 ml of a 20 per cent solution can be injected intravenously within ½ to 1 min (Zwillinger, Boyd and Scherf) The injection is accompanied by a sensation of warmth and can be followed by a significant drop in blood pressure. Before the end of the tachycardia, conduction disturbances and ventricular extrasystoles may occur With severe myocardial damage and intraventricular conduction disturbances, magnesium sulfate should be avoided.

Procaine amide (Pronestyl) is similar in action to quinidine It is especially indicated in ventricular tachycardia but has been recommended also in supraventricular tachycardia. According to Bellet and coworkers (1952), it is effective in 80 per cent of the cases.

Sedatives with sympatholytic action have been used (Szutrély and Voltay) One mixture is the so-called "*lytic cocktail*" of Laborit and Huguenard, which is composed of Largactil/Phenergan/Dolantin in the ratio of 1:1:2 and is given intravenously at an approximate dosage of Largactil of 0.6 mg/kg.

Sympathomimetics, like *Neo-synephrine,* are occasionally effective This illuminates the multiple influences which are possible. The sympathicomimetics stimulate the carotid sinus through a blood pressure rise and thus produce vagal stimulation. In case 0.5 mg intravenously does not work, a double dose can be tried, except in cases of hypertension and coronary sclerosis (Youmans and coworkers).

Other drugs have been used occasionally but have no practical importance They are *adenosine* (Kalaja), *fagarine*[1] (Scherf et al, 1949, Silver and Weinberg; Taquini), *Veratrum viride* (Shaw), *calcium gluconate* (Wolffe and Bellet), *Atabrine* (Gertler and Yohalem).

Surgical procedures have been attempted in patients with a great frequency of attacks. Leriche et al. (1935) recommended *left stellectomy.* According to White and Bland, the ganglion chain should be removed bilaterally from the stellate ganglia downwards to the fourth or fifth thoracic ganglion. *Alcohol injection* into the ganglia can be effective, but the attacks may recur after regeneration of nerve fibers (Coleman and Bennett).

PROPHYLACTIC MEASURES FOR THE PREVENTION OF ATTACKS. When any precipitating factor is known in a particular case, such as overeating, alcohol, smoking, coffee, constipation, certain body positions, or psychic stimulation, it should be eliminated.

In resistant cases, *medical means* should be added. The same drugs which have been described to terminate an attack can be given in small doses for this purpose. Basically, the smallest dose which may prevent an attack should be used.

Of the *vagomimetics,* particularly good are *Doryl* or *Mestinon* in tablet form. It is recommended to begin with three tablets daily.

Digitalis is the drug of choice if the attack has not occurred under previous digitalization, and if heart failure is present

Quinidine is to be recommended in patients without heart disease. Association with phenobarbital often proves useful

Procaine amide with an initial dose of 250 mg three to four times, is also to be considered.

Rauwolfia alkaloids are not effective in terminating an attack but may be effective prophylactically. *Serpasil,* 0 1 mg, three to four times daily is the usual dose for children, 0.25 mg three to four times daily for adults (Bixby, Szutrély and Voltay).

[1] Fagarine may cause ventricular fibrillation and should not be used in clinical cases. *Editor.*

in chronically ill cardiac patients in the hospital

The attacks are favored by advanced age. While some cases have been observed in the second decade, most of them occur between 50 and 70 years of age

The *male sex* predominates, about two-thirds of the cases occur in males.

Ventricular tachycardia can occur either with sinus rhythm or with fibrillation. Exceptionally, it can also follow a supraventricular tachycardia (Barker, P S).

Usually, though not always, the attacks occur in patients with a severely damaged myocardium; in about one-half the cases, the clinical picture of congestive failure either exists or supervenes

In a statistical study of 107 cases of paroxysmal ventricular tachycardia, Armbrust and Levine found the following·

Finding	*No of Cases*
Coronary artery disease	79 (74%)
Rheumatic heart disease	9
Congenital heart disease	1
Wolff-Parkinson-White syndrome	5
No evidence of heart disease	13 (12%)

During *severe infections*, such as diphtheria, rheumatic fever, or streptococcal infections, ventricular tachycardia may be observed in children

Epinephrine and large doses of quinidine or *Pronestyl* can provoke attacks

Overdose of *digitalis glycosides* may precipitate ventricular tachycardia, and even moderate doses may do so in a severely damaged myocardium This is not astonishing, for digitalis favors the formation of ventricular pacemakers Since digitalis intoxication in normal individuals does not cause ventricular tachycardia, preexisting myocardial damage is essential in the causation of this disturbance

According to general experience, patients with an otherwise normal heart were encountered mainly in the younger age groups Campbell and Elliot found an apparently normal heart in 8 of 11 patients under 40 but in only 2 of 31 patients over 40 years of age

The following etiologic-clinical classification of the ventricular tachycardias is after Froment

1. *Ventricular tachycardia in cases with severe myocardial disease*
   a. *Cases with septal lesions.* They usually follow a recent myocardial infarction involving the septum, but may occur without it. Rarely they are due to syphilitic myocarditis involving the septum. They occur mostly in advanced age, and the ECG usually has a constant configuration. The prognosis is rather poor.
   b. *Cases with terminal, prefibrillatory tachycardia.* This form is observed in patients with severe congestive failure, often follows previous brief runs of tachycardia, and is revealed by a polymorphic aspect in the ECG. The prognosis is very poor.
2. *Ventricular tachycardia in clinically normal hearts·*
   a. *Extrasystolic type (extrasystolie ventriculaire en salves,* Gallavardin) with onset during youth and with a course which may be either benign or obstinate, even lasting for more than 30 years.
   b *Essential type* (Bouveret-Hoffmann), with less frequent but longer attacks, which usually begin during youth and which may have a course of many years The prognosis is good.

Mechanism. The possibility of a circus movement cannot be admitted because there are no pathways between the ventricles The cases which present ventricular extrasystoles between attacks having the same coupling and pattern confirm that both the tachycardia and the extrasystoles have the same mechanism, i e, a heterotopic focus of impulse formation or a reentry phenomenon.

Pathology. Upon gross examination, there is no typical finding in cases of ventricular tachycardias However, lesions of the ventricular septum are rather frequently encountered, and microscopic lesions consisting of inflammatory or degenerative changes in the network of Purkinje or in the AV node, the bundle of His, and its branches are extremely frequent (Mahaim, 1932). It is logical to consider that these lesions represent the anatomic basis of the attacks of tachycardia. This assumption explains why not infrequently ventricular tachycardia and AV block release each other The former corresponds to a stimu-

which periodically increase and decrease in amplitude independently of the respiration. These pulsations will be revealed even better, however, by recording a *jugular tracing* and are due to superposition of the A and C waves.

The changes of *heart size, stroke volume,* and *blood pressure* are the same as in supraventricular tachycardia. During the clinical taking of blood pressure, a periodic increase of the pulse can occasionally be demonstrated (see above).

With the auscultatory method, arterial sounds are generally audible only at long intervals corresponding to a periodically increased systolic pressure. With the oscillometer, this phenomenon is designated as "nonalternating anisosphygmia" (Lian et al., 1931).

The effect of the tachycardia on the peripheral circulation is in general more severe than in supraventricular tachycardia because usually the heart is damaged Somnolence and Cheyne-Stokes respiration are more frequently observed. Exceptionally, tachycardia may be followed by gangrene of the fingers or toes (Abrahams).

The Electrocardiogram. The typical picture of ventricular tachycardia shows ventricular complexes similar to ventricular extrasystoles in rapid and regular (or almost regular) sequence; *there are P waves recurring at a slower rate* (Fig. 11-3B, C). The shape of the ventricular complexes in the various leads depends upon the site of the ectopic pacemaker, as in the case of extrasystoles For their recognition, the same methods should be employed. Theoretically, the tachycardia could originate in the basal portion of the ventricular septum or at the origin of the bundle of His, so that a normal pattern of ventricular stimulation could occur. Furthermore, the P waves can be absent if there is atrial fibrillation in addition to the ventricular tachycardia.

If the demonstration of a rapid ventricular rate, independent of SA stimulation, cannot be obtained, finding the same coupling for extra-

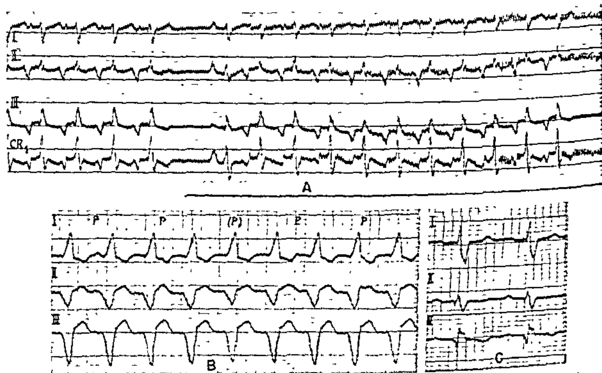


Fig. 11-3. A Supraventricular tachycardia in an 8-year-old girl Obstinate and frequent attacks. Inverted P waves in leads II, III, and CR_1 Because the AV interval is 0.14 sec, the pacemaker must be in the caudal portion of the atria With carotid sinus pressure (white flap), the tachycardia can be interrupted for short periods. However, after one ventricular complex of sinus origin, the attack starts again. B. Ventricular tachycardia in a 75-year-old man with a myocardial infarct. For 4 days there was a right ventricular tachycardia at a rate of 133. The P waves fall before, within, or after the QRS complexes at a rate of 70. C. Same case as in (B), after Pronestyl (0.5 Gm, four times). Sinus rhythm at a rate of 70, prolonged AV conduction, and right bundle branch block.

should be given with the blood pressure under continuous control and the ECG under constant observation. The *injection* of 1 Gm should be given *very slowly* (at about 0.1 Gm every 2 min). If the attack is terminated after only part of the above dosage is given, the administration can be discontinued The injection should be interrupted if the ECG shows evidence of a definite increase in the *duration* of the QRS complex or if there is a significant drop in *blood pressure.* Since several fatalities have been *reported* following the intravenous administration of Pronestyl (generally with rapid administration), the intramuscular injection is preferred in several institutions as being less dangerous For this, 0 5 to 1 0 Gm is injected, and the injection can be repeated one to *three times* at 1- to 4-hour intervals until the *tachycardia* is controlled If there is no special cause of worry, the oral route can be employed With doses of 0 5 Gm every 2 hr, or 1 Gm every 4 hr, the attack may be terminated within a period varying from hours to days in about 70 per cent of *cases* (*Bellet et al*, 1952).

Quinine, quinidine, and Pronestyl are contraindicated in cases where there has been an AV block.

Digitalis favors the formation of ectopic foci in the ventricles. However, it is occasionally capable of causing the disappearance of a ventricular tachycardia, *apparently by improving the circulation*, through a prolongation of the refractory period, and through a decrease of conduction (Scherf and Kisch, Gilson and Schemm) Obviously, this drug cannot even be considered if the attack has occurred while the patient is under digitalis therapy or in a *prefibrillatory state with multifocal ventricular* complexes If this is not the case and heart failure is present or there is low blood pressure, digitalis can be used

Potassium salts, on the contrary, are specifically indicated in paroxysmal ventricular *tachycardia favored by overdigitalization,* because *during toxic digitalis action, an intracellular decrease of potassium and magnesium ions occurs* Under such conditions, an attack can be terminated by the administration of 2 Gm potassium chloride or citrate every 2 hr or by the careful intravenous infusion of an isotonic potassium chloride solution *Overdosage* should be prevented by determination of the serum potassium levels and through observation of the ECG.

Magnesium sulfate is similarly worth a try, particularly in ventricular tachycardia under the effect of digitalis (Zwillinger, Boyd and Scherf; *Szekely and Wynne*). As with premature *beats* caused by digitalis, 15 to 20 ml of a 15 to 20 per cent solution of magnesium sulfate should be injected slowly into a vein.

Morphine has been recommended by Gonzalez Sabathié (intravenous injection of 10 to 40 mg); *papaverine* has been advocated by Elek and Katz.

Atropine. *Atropine sulfate* (1 to 2 mg, intravenously *or intramuscularly*), alone or in combination with quinidine, has also been successful in some cases (Salley; Levine, 1945). Atropine is generally administered only when the ventricular rate has already significantly decreased through the use of quinidine. Its action seems based on a *prolongation* of the refractory period.

COMPLICATIONS OF THE PAROXYSMAL TACHYCARDIAS

Heart failure can be induced by prolonged attacks of the rapid forms of tachycardia. This occurs particularly in ventricular tachycardia when the heart has been previously damaged *Pulmonary edema (possibly associated with pulmonary infarction)* and hepatic engorgement, followed by abdominal distention and ascites, usually disappear rapidly after the end of the attack, unless the previous cardiac condition was too poor. Cardiac glycosides may be necessary but should be administered with caution.

A *myocardial infarct may be the result of a* prolonged paroxysmal tachycardia in *cases* with coronary stenosis Precordial pain can reveal this occurrence, although such pain may be absent if there is a simultaneous onset of failure After each prolonged attack of tachycardia, one should examine the temperature, white cell count, blood pressure, transaminase *activity, sedimentation rate*, and ECG, in order to exclude the occurrence of a *myocardial infarct.*

Electrocardiographic evidence of *coronary insufficiency* may last from minutes to hours after the attack is over and is present particularly *in cases* with poor coronary flow and ventricular *hypertrophy* or other myocardial le-

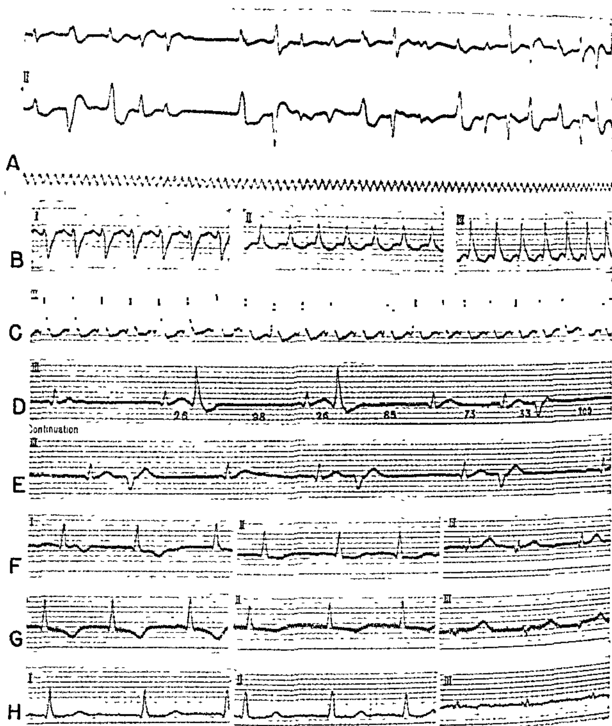


Fig. 11-5. A Complete ventricular anarchy in a woman, aged 60, who was suffering from chronic rheumatic carditis and circulatory failure (autopsy was performed 3 days later). Atrial fibrillation. Complexes of supraventricular origin (first and sixth) with variable ventricular conduction paths; ventricular tachycardia with irregular complexes. B. Left-sided ventricular paroxysmal tachycardia in a 50-year-old woman with myocardial disease of unknown origin. During the attack: ventricular rate, 227 C Immediately following intravenous injection of quinine hydrochloride, gr 7½ (0 5 Gm); ventricular rate, 240 Variable irregularities in the S-T segment suggest atrial fibrillation D. 40 sec later; atrial fibrillation. Marked abnormality of the ventricular complexes at irregular intervals, with ventricular extrasystoles. E 5 min later atrial fibrillation with myocardial damage, particularly of the left ventricle. F. 2 days later; ventricular complexes even more abnormal. G. 4½ months later; atrial fibrillation. Regression of posttachycardia syndrome. (*From Holzmann. Klinische Elektrokardiographie, 1955.*)

3

Extrasystoles

DAVID SCHERF

Extrasystoles are contractions of the whole heart or parts of the heart elicited by the preceding beat and therefore bound to it by a fairly constant interval (*constant coupling*). They are often called *premature contractions*. However, in atrial fibrillation, some of the beats conducted from the atrium are more premature than are the extrasystoles On the other hand, *extrasystoles may not* be premature when they appear late in diastole and excite only part of the heart while the rest is excited by the normal impulse The above definition excludes ectopic extra beats caused by *automatism of deeper centers* (*idioventricular* or parasystolic beats). The former come late in diastole, the latter appear in all phases of diastole and therefore do not have a fixed coupling

HISTORICAL REMARKS

The "skipping of the heart beat," caused by an extrasystole, and the intermittent pulse were known to physicians for many centuries The Chinese discussed them thousands of years ago With rare exceptions (see Chinese medicine) this phenomenon was considered to have a bad outlook Only at the very end of the nineteenth century did Cushny and Wenckebach simultaneously discover that the intermittent pulse is in most cases caused by extrasystoles, for the first time they described correctly this arrhythmia in man

TYPES

Extrasystoles are divided into different groups depending on the part of the heart from which they originate While under normal conditions, impulses are formed only in the so-called specialized tissue ("specialized fibers") which alone has automaticity or the ability to form impulses (SA node, AV node, bundle of His, bundle branches and ramifications), under abnormal conditions, extrasystoles may originate in the common muscle fibers One can elicit extrasystoles from any part of the atria or ventricles by local application of aconitine, digitalis, strophanthin, or hypertonic solutions of sodium chloride and barium chloride The problem is not definitely solved because it is impossible to decide by histologic methods how far the specialized tissue reaches. It seems, however, improbable that the extrasystoles and atrial tachycardias which appear on application of aconitine on the tip of the left atrium could be caused by firing off of impulses in specialized fibers.

COUPLING

The length of the coupling in a given patient varies little, differences usually amounting only to 0 02 to 0 04 sec. Most often the duration of the coupling is around 0.32 sec, but it may be longer, rarely shorter (0 28 sec). Lewis called the coupling "the forced cycle," as it is ended by the forced beat or extrasystole The duration of the coupling may be influenced by drugs, such as quinidine, or by the appearance of bundle branch block.

VENTRICULAR EXTRASYSTOLES

These are recognized in the electrocardiogram as premature ventricular complexes, usually of abnormal form. Only rarely do these extrasystoles show a ventricular complex of

tricular tachycardia, if several stimuli are conducted one after another, and cause a functional bundle branch block.

MOBITZ'S INTERFERENCE DISSOCIATION. A pararrhythmia of sinus and node activity with additional *functional bundle branch block* can be recognized because the prematurely conducted ventricular impulses also show the bundle branch block pattern.

Not infrequently, a definite decision as to the underlying mechanism cannot be made from a single ECG finding. Then, the following methods may be used:

1. *Reflex vagal stimulation* This barely influences ventricular tachycardia, or affects it not at all, whereas it may terminate supraventricular tachycardia (a functional bundle branch block would disappear), or so depress AV conduction that AV block occurs (the rapid atrial activity becomes visible) and fibrillation or flutter waves are unmasked.

2. *Esophageal leads* may clarify the relationship of the ventricles and atrial complexes by revealing the latter with a higher voltage.

3 *Pronestyl* can contribute to the diagnosis by overcoming a ventricular tachycardia

The *differential diagnosis* between supraventricular and ventricular tachycardia can be made, up to a certain point, by observing the characteristics of the rhythm, the heart sounds, the arterial and venous pulses and, above all, through the electrocardiogram. Reflex vagal stimulation can be informative (Table 11-1).

Occurrence. Paroxysmal ventricular tachycardia is rare in office practice, but it is often encountered during acute heart attacks and

TABLE 11-1 DIFFERENTIAL DATA OF THE TACHYCARDIAS

	Supraventricular	*Ventricular*
I Rhythm	A *Regular* (essential type) Exceptions—irregular with· 1. Second-degree AV block 2 AV tachycardia with interference dissociation B *Irregular* (extrasystolic type)	A *Either regular or slightly irregular* (essential type) B. *Severely irregular* (extrasystolic type)
II. Auscultation	First heart sound of constant loudness (may not be so in I A.)	First heart sound periodically increased (except with retrograde atrial stimulation or atrial fibrillation)
III Arterial pulse	Equal	May be periodically increased
IV. Jugular tracing	Constant large pulsations (may not be so in I A)	Periodical atrial waves (except that retrograde atrial stimulation will cause nonperiodic waves while atrial fibrillation will cause their disappearance)
V Electrocardiogram A Atrial complex	*P wave in constant relationship to the ventricular complexes* (except in the presence of block and in AV tachycardia with interference dissociation)	*P wave independent of the ventricular complexes* (except with retrograde atrial stimulation; the P waves will be absent if there is atrial fibrillation)
B. Ventricular complex	*Ventricular complexes of conducted type* normal QRS duration (except if there already is bundle branch block or if a functional bundle branch block is caused by the tachycardia)	*Bizarre ventricular complexes,* QRS interval prolonged and deformed (except if the stimulus originates in one stem of the [illegible] lation with a functional bundle branch block, and tachycardic atrial fibrillation with conduction through an abnormal AV pathway (Wolff-Parkinson-White syndrome)
VI Reflex vagal stimulation	Often effective by: A Terminating the attack B. Blocking the AV conduction (rare)	Ineffective

normal systole (Fig. 11-7G). The next normal beat following the extrasystole is not disturbed and comes at the exact moment it would have come had there been no extrasystole (*compensatory pause*).

An interesting phenomenon has been seen in diseased hearts: the T wave of the first postextrasystolic beat may be abnormal, becoming flat or even inverted, particularly in leads V_3 or V_4

Under abnormal conditions, particularly in elderly patients, the first postextrasystolic beat is an "escaped" idioventricular beat from a deeper ventricular center (Figs. 11-7B, 11-9B).

If every beat of the basic rhythm is followed by an extrasystole, there is a *bigeminal rhythm;* if two extrasystoles follow each normal beat, a *trigeminy* is present A succession of many extrasystoles (Fig 11-7D, E) may also be called a *paroxysmal tachycardia.*

Even if extrasystoles continue to occur for many years, they show in the most minute detail the same electrocardiographic pattern, as long as the heart remains healthy and they originate in the same focus If the extrasystoles are *polyfocal* or *multiform* (Fig 11-7C, D and 11-9B), they are definitely significant They originate in several foci and spread over the heart in different patterns When several centers exist, one may conclude that several abnormally functioning fibers are present, therefore, *multiform extrasystoles indicate heart disease* They are seen in the different forms of *myocarditis* and most frequently in coronary heart disease (Fig 11-9B)

One should be aware, however, that extrasystoles may be the consequence of *digitalis* action, regardless of how small a dose the patient may be getting They may appear even after a single dose of 0 3 Gm standardized powdered leaves of digitalis After digitalis is discontinued, they may persist for 2 to 3 weeks On the other hand, they were absent in several instances of suicide with digitalis Experimental and clinical data indicate that they appear in digitalized hearts that are exhausted or damaged and *in which the potassium content of the muscle is diminished* The appearance of multiform ventricular extrasystoles during the administration of digitalis is a phenomenon of great importance, as most of these patients develop more and more extrasystoles if digitalis is continued, ultimately, ventricular tachycardia may appear with alternating or continuously changing ventricular complexes Such tachycardias may also appear spontaneously in patients with damaged myocardium (Fig 11-7E).

ATRIAL EXTRASYSTOLES

Extrasystoles originating in the atria are recognized in the electrocardiogram by the appearance of *premature P waves* which, in most instances, have a different form than in the existing sinus beats They may be inverted, higher or shorter, differently slurred, or notched. Because of their prematurity, these P waves are often hidden in the preceding T waves and may be recognized only by the change of form of the T waves. In continuous bigeminy, every T wave contains a P wave, so that there is no possibility of comparing them with normally shaped T waves; the diagnosis is then difficult (Fig. 11-8B). Too often, in the absence of a clear P wave, the diagnosis of an AV extrasystole is made and it is presumed that the atrium and ventricle contract simultaneously. Atrial extrasystoles on their way down to the ventricles may find the path blocked by refractory tissue from the preceding systole, and therefore will not be followed by a ventricular contraction. These are called *blocked atrial extrasystoles* (Fig. 11-8C); often, for the same reason, the spread of the atrial extrasystole is abnormal within the ventricles (*aberrant atrial extrasystoles*). This happens even in healthy hearts and has no special significance (Fig. 11-8C). Atrial extrasystoles are followed by *a pause which usually is noncompensatory*

If atrial extrasystoles are *multiform,* atrial fibrillation usually follows, such abnormalities are often seen in the elderly patient and are an indication for therapy with quinidine

EXTRASYSTOLES FROM THE BUNDLE OF HIS

These extrasystoles are rare (Fig 11-7A). They are characterized by premature ventricular contractions showing the same ventricular complexes as the existing sinus rhythm.

SINOATRIAL NODE EXTRASYSTOLES

These extrasystoles are also rare, but they have been studied experimentally and a few typical instances have been observed in man. They are characterized by premature P waves exhibiting the same form as the P waves of

lation, the latter to a functional depression of the conducting system. Observations in cases with myocardial infarcts reveal that the ventricular septum is a preferred site from which ventricular tachycardia can be elicited. It is not known how far the histologic changes that produce ventricular tachycardias spread into the periphery.

There is, so far, no anatomic proof of congenital abnormalities in cases of obstinate extrasystolic tachycardias with good prognosis (Parkinson and Papp).

Prognosis. The prognosis of ventricular tachycardia depends primarily upon the underlying cardiac condition. It is severe in patients where the attack is provoked by a *fresh myocardial infarct.* Among 42 such patients of Armbrust and Levine, 28 (or 64 per cent) died within 1 month, 10 lived longer than 2 years, and the longest survival was for 11 years. The outlook has considerably improved with modern therapy, including anticoagulants, treatment of shock, and treatment of the tachycardia itself, *if immediate treatment is given.* Even today, prognosis is severe for patients who have a cardiogenic shock during the attack of tachycardia. The same is true for the ventricular tachycardia during infections, because the attack reveals the existence of myocarditis The outlook is extremely poor if the ventricular tachycardia occurs during an advanced stage of *heart failure.* In younger patients, this is usually due to chronic myocarditis; in older cases, the underlying basis is generally a degenerative process due to coronary heart disease (and often an old infarct). The designation of these types as *terminal* reveals their prognosis According to Strauss, 80 per cent of such patients die within 24 hr, according to Cooke and White (1943), one-half of such patients die within the first 3 weeks and the other half within the next few months, the longest survival being for 18 months. The immediate prognosis is somewhat better if the paroxysmal tachycardia occurs during therapy with digitalis glycosides. Then, discontinuance or modification of therapy can affect the tachycardia. Even so, the outlook remains poor on account of poor myocardial conditions.

In relatively rare cases with *apparently normal hearts,* the prognosis is considerably better, though occasional fatalities during an attack occur even in such cases, apparently through transformation of the ventricular tachycardia into flutter and then fibrillation

Treatment. Certain measures effective in supraventricular tachycardia are also effective in the ventricular form; others, however, fail. Certain medications are specifically indicated in ventricular tachycardia. Since the prognosis becomes worse with prolongation of the attack whenever the heart is damaged, treatment should be instituted immediately.

Reflex vagal stimulation and parasympathomimetic drugs are worthless, as they do not influence a ventricular ectopic focus. In spite of this, carotid sinus pressure should be tried in order to exclude a case of supraventricular tachycardia with an equivocal ECG picture. If unsuccessful, it will confirm the diagnosis of a ventricular form. On the other hand, no time should be lost while trying vagal stimulating drugs.

Quinidine can be tried as in supraventricular tachycardia. If the general conditions are severe, one should not wait for the effect of an oral therapy but should employ, instead, a more rapidly acting intravenous preparation: *quinidine lactate,* 0 6 Gm in 200 ml of 5 per cent glucose at a speed of 2 to 3 ml per min (Kantner), or *quinidine gluconate* or *hydrochloride,* 0.3 to 0.8 Gm in 20 to 100 ml of isotonic saline solution injected through not less than 10 min (Bellet et al., 1949), or a slow injection of *quinidine dihydrochloric carbamide,* 0.3 to 0.5 Gm The heart action should be monitored during these injections, and administration of the drug should be discontinued as soon as the tachycardia is terminated. Quinidine can be given by the intramuscular route, using about twice the above dose and repeating this dose, if necessary, at hourly intervals.

Procaine amide (Procaine amide hydrochloride, *Pronestyl*) has occasionally proved superior to quinidine, even though it has basically the same mode of action. As a result, this drug has become the drug of choice in ventricular tachycardia. When special haste is indicated, i e, if the attack lasted more than 12 hr, a fresh myocardial infarct has occurred, or there is severe congestive failure, Pronestyl can be given intravenously. Since it has a hypotensive action, this method of administration is *not* recommended if the blood pressure is already very low. In all cases, the injection

are excited simultaneously, in this case the P wave is hidden in the QRS complex. In another form, the premature P wave precedes the QRS complex by an interval which is *shorter* than the normal P-R interval of the patient. These P waves are very low and positive in lead I, peaked, of short duration, and deeply inverted in leads II and III; they are positive in aVR and inverted in aVF In a third form, the abnormal P wave appears after the QRS complex, usually between the QRS complex and the T wave (Fig. 11-8A).

With certain, well-studied exceptions, the first-named form originates *in the middle part* of the AV node, the next one *in the upper (atrial) part*, and the last one in the *lower (ventricular) portion* It seems that premature inverted P waves with a normal P-R interval may originate in the so-called *coronary sinus node*, an extension of the AV node to the orifice of the coronary sinus For one or several beats following atrial extrasystoles, the P waves of the regular rhythm may show an abnormal form (Fig 11-8D); there is so far no satisfactory explanation for this phenomenon, which is not rare

RETURN EXTRASYSTOLES

These rare extrasystoles may be subdivided into several forms One of them has been well analyzed experimentally but has not been observed in clinical cases. If ventricular extrasystoles are initiated by any method in the dog, they often are conducted backwards into the atria (*retrograde conduction*) If the last of a series of extrasystoles reaches the atria, it is followed by a beat of normal form, and analysis shows that the extrasystolic impulse, while on its way to the atria, has *returned to the ventricles* In another form of the same phenomenon also observed in man, *return extrasystoles* are seen in the type of AV rhythm in which the P wave is present between the QRS complex and the T wave Thus in Fig 11-8E, obtained in an experiment in a dog, all beats with such P waves are followed by a return extrasystole Since one cannot assume that the part of the AV system above the bifurcation which had just conducted the impulse to the atria is able to conduct it immediately down again to the ventricles, one must assume a longitudinal dissociation of the AV system permitting retrograde conduction in one part, normal conduction in another.

EXTRASYSTOLES DUE TO DRUGS AND DIFFERENT COMPOUNDS

Extrasystoles are frequently the consequence of drug action. They may appear sometimes in dangerous numbers and may lead to fatal ventricular fibrillation The most important compounds are listed below.

Digitalis extrasystoles have been mentioned above; it may be stressed again that in the healthy person and in most patients with abnormal hearts such extrasystoles do not appear even after administration of large doses. They appear in experimental animals only before death but are easily elicited if digitalis or strophanthin is applied locally to the cardiac surface (Fig. 11-9A). They are particularly common in the hypertrophied and dilated hearts of rheumatic mitral lesions or coronary sclerosis; investigations have demonstrated a diminished content of potassium in the muscle fibers of these hearts.

Digitalis extrasystoles frequently show differences of form, which may be only slight or very marked.

Quinine, quinidine, and Pronestyl are known to elicit extrasystoles and dangerous tachycardias, as well as fibrillation, in man and in the experimental animal. Their use in combination with certain anesthetics is dangerous

Chloroform and cyclopropane both cause extrasystoles of varying form. The appearance of extrasystoles in anesthesia with cyclopropane is less dangerous than with chloroform. Why cyclopropane occasionally leads to so many extrasystoles and why they do not occur in other cases, is unknown *Trichloroethylene* has a similar action

Epinephrine, caffeine, and *nicotine* often elicit extrasystoles.

CLINICAL DATA

Incidence. Extrasystoles are common in the healthy person. They appear so often that the statement has been made that no adult escapes them permanently. In most people, they are asymptomatic. Extrasystoles appear in all ages and have been often heard on auscultation of the fetal heart. It is not decided as yet whether atrial or ventricular extrasystoles are more common, but in early youth, the atrial type seems to predominate.

Different statistics compiled on different material (hospital patients, patients with heart

sions, being more pronounced and more lasting for attacks of long duration.

Emboli in the greater or lesser circulation can occur after a prolonged attack if a cardiac thrombosis has occurred during the tachycardia.

POSTTACHYCARDIAL SYNDROME

The *posttachycardial syndrome* consists of ECG changes of the ST-T segments which follow paroxysmal tachycardia continued for several days, and which persist from a few days up to 8 weeks. The longer the tachycardia has lasted, the more likely it is for these changes to occur, and the longer they will persist. They consist often of pronounced inversion of the T wave in several leads, which usually makes it possible to localize the disturbance in either the left or the right ventricle. The QRS complex is usually not involved (Fig 11-5B–G). The inverted T wave is generally less pointed than in myocardial infarction, the Q-T interval is prolonged initially. This picture is less common after a supraventricular than after a ventricular tachycardia. This supports the idea that the abnormal T waves reveal damage of that ventricle from which the tachycardia had its origin (Gallavardin, Graybiel and White, Cossio et al.) This phenomenon may occur in otherwise normal cases.

The *symptoms* of the patient are overshadowed by lassitude, especially after a prolonged attack. A transient slight cardiac dilatation has been observed (Cossio et al).

The ECG picture may be considered as evidence of fatigue of the ventricular myocardium resulting from the prolonged tachycardia The metabolism is altered by the uneconomical tachycardia—more altered if the myocardium was damaged before the attack

The *evaluation of the ECG* requires great care, and the following points should be considered:

1. The ECG alterations may be considered evidence of a posttachycardial syndrome only if they were *not* present prior to the attack. Ventricular tachycardia may mask the pattern of an abnormal ECG.

2. If the attack was associated with precordial pain, or if heart failure followed it, one should consider the possibility that there has been a *myocardial infarct.* The clinical data may help in the differential diagnosis, although their absence does not rule out a small infarct. Changes of the QRS complex that were not present before the attack, or the onset of a monophasic wave with elevation of the S-T interval in certain leads, speak for a *fresh myocardial infarct.*

3. If the inversion of the T wave is found chiefly in the chest leads V_1 to V_3, one should consider *acute cor pulmonale* (pulmonary infarct caused by embolism).

4. If the attack was treated with large doses of digitalis glycosides, the typical "digitalis effect" of the ECG is to be expected Quinidine or Pronestyl may cause flattening of the T waves, possibly associated with broader U waves, and occasionally with a prolongation of the QRS complex.

Little is known still about the *pathologic anatomy* of the posttachycardial syndrome. At autopsy of one case, moderate hypertrophy and dilatation of the heart were found, without any other evidence of myocardial lesions (Cossio et al)

In general the *prognosis* is good Even so, occasionally, and without any apparent particular reason, a fatality may occur during an attack.

The abnormal metabolic state of the heart requires physical rest and good nutrition Since the nature of this metabolic disturbance has not been clarified, more definite therapeutic measures cannot be used However, adequate supply of glucose, potassium, vitamins, and possibly metabolic enzymes is indicated; there is no indication for cardiac glycosides.

are excited simultaneously, in this case the P wave is hidden in the QRS complex. In another form, the premature P wave precedes the QRS complex by an interval which is *shorter* than the normal P-R interval of the patient These P waves are very low and positive in lead I; peaked, of short duration, and deeply inverted in leads II and III, they are positive in aVR and inverted in aVF. In a third form, the abnormal P wave appears after the QRS complex, usually between the QRS complex and the T wave (Fig. 11-8A).

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Different statistics compiled on *different material* (hospital patients, patients with *heart*

the same form as the normal complexes; this is the case only when they originate in the bundle, above the bifurcation (Fig. 11-7A). In most instances the QRS complexes and T waves are abnormal, because the stimulus originates in one of the ventricles and consequently spreads abnormally. The QRS complexes may be widened, slurred, and notched; the T waves are often oppositely directed (Fig. 11-7B, D) Sometimes, particularly when the basic rhythm is slow, an extrasystole is sandwiched between two sinus beats without disturbing the existing rhythm; this is called an *interpolated extrasystole* (Fig 11-7F). Usually, however, at some time during the extrasystolic contraction, the next normal atrial contraction occurs but cannot be conducted to the ventricles because of the refractoriness caused by the extrasystolic contraction. Thus an extrasystole replaces, so to speak, a

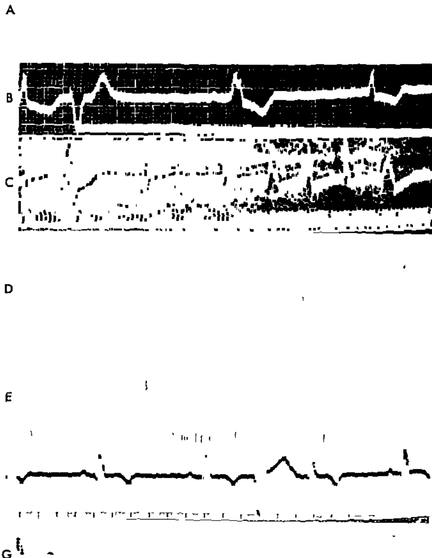


Fig. 11-7. A. Lead III. Prolonged P-R interval in a patient with left bundle branch block; a ventricular extrasystole arises above the bifurcation of the AV conduction system. B. Lead III. Atrial fibrillation, digitalis effect, and ventricular extrasystole, followed by an ectopic, idioventricular, automatic beat. C. Lead III. Atrial fibrillation with multiform ventricular extrasystoles. D. Lead III. Complete AV block; an automatic beat is followed by a series of ventricular extrasystoles which are multiform. E. Lead III. Groups of ventricular extrasystoles with alternation of form. No digitalis had been given. In the vast majority of the cases, such an arrhythmia is the consequence of administration of digitalis. F. Lead III. Interpolated ventricular extrasystole in a patient with posterior infarction. G. Lead I Ventricular extrasystole. The normal P wave is visible between the QRS complex and the T wave of the extrasystole.

tressing than the usual ones It is typical for these sensations to come mostly at rest, which is the time extrasystoles most often occur, chiefly on account of slower rate.

Other patients complain of *dizziness or even of fainting* Questioning elicits that this dizziness lasts only "a second" The reason for the vertigo in the absence of a long cardiac standstill is not known

Pain is a not infrequent complaint It may be "knifelike" or stabbing, and its brevity alone speaks against coronary involvement. Often it is not the *extrasystole itself which causes* palpitation or pain but the first postextrasystolic beat with its larger stroke volume.

Some patients with extrasystoles have a most interesting *cough reflex*. The cough appears simultaneously with the extrasystoles, comes from "nowhere," and may be very annoying The mechanism is not clear, but the presence of a *reflex from the heart or the* pressoreceptors to the respiratory *tract is obvious*

All these sensations are aggravated if the patient feels his pulse and finds it intermittent

Signs. Most extrasystoles are diagnosed by auscultation; the heart tones of the premature contraction followed by a pause are heard However, without an electrocardiogram mistakes, although rare, can occur, since dissociation with interference, parasystole, or even a periodically dropped beat may lead to a similar auscultatory impression The 1st sound of the extrasystolic contraction is often accentuated, the 2d sound *may be absent* (Fig 11-8F)

The pulse "skips," as it does in periodically dropped beats, in bigeminy, the extrasystoles may be so premature that their pulse waves are not transmitted to the periphery because of the small output this is the "pseudobradycardia" of our *forefathers*

Extrasystoles may also give the *impression* of a gallop rhythm, since the two sounds of the beat preceding the extrasystole are occasionally followed by the only sound produced by the extrasystole

PROGNOSIS

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[illegible] over a period of years, they do not lead to complications and can be ignored On the other hand, *extrasystoles* can elicit fibrillation and, if the ventricles are involved, *sudden death. This* happens when extrasystoles occur *extremely early, during* the last few hundredths *of a second* of the T wave of the preceding beat (Fig. 11-12C). If a premature impulse reaches the heart during this phase, the so-called *critical or vulnerable phase,* it leads to rapid firing of impulses resulting in multiple extrasystoles, flutter, or fibrillation. *This does not happen* under normal conditions but *occurs when the* heart is in an "*abnormal metabolic*" state, *for* instance when there is abnormal excitability of a center because of lack of potassium or calcium This is why extrasystoles during chloroform anesthesia and those in acute myocardial infarctions bring so great a potential risk.

THERAPY

When extrasystoles appear, a thorough examination is indicated. If the patient is not aware of the existence of the arrhythmia, it is best not to mention it If he becomes aware of it, he is often disturbed, since for the layman an irregularity of the pulse seems to herald the threat of a cardiac catastrophe. Reassurance and explanation of the phenomenon may help *in many cases It may* be of value to point out to the patient that *no restriction* of activity is required and that he may lead a normal life

The treatment with drugs is reserved for those patients discussed above in whom the extrasystoles create some risk and for those who *complain* that the arrhythmia disturbs them The treatment *of choice* is *quinidine*, which is given three to six *times* daily *in* the form of tablets containing 0 2 Gm, after a test dose of 0 2 Gm Most extrasystoles, but by far not all, disappear with this medication If hypersensitivity prevents the use of quinidine, *one may use Pronestyl,* 0 75 Gm (three capsules), three to *four* times daily While ventricular extrasystoles *respond* well, the atrial type is less frequently influenced

The administration of 4 to 8 Gm daily *of potassium chloride* helps, particularly in digitalis-induced extrasystoles, but this therapy is to be used only if renal function is normal, because it carries the danger of other disturbing arrhythmias. Digitalis therapy often abolishes extrasystoles not caused by this medica-

the existing sinus beats; often, but not invariably, they are followed by a pause which is *shorter* than that necessary to create a normal P-R interval. The rarity of these extrasystoles and of those from the bundle of His and the AV node is understandable if the following law is considered: centers with highly developed automaticity, i.e., with the ability to form impulses, rarely show abnormal beats of the extrasystolic type; however, centers in the peripheral ramification of the nodes or in the Purkinje system more often exhibit their abnormal extrasystolic impulses.

ATRIOVENTRICULAR (NODAL) EXTRASYSTOLES

These extrasystoles may be divided into three groups. In one, the atria and ventricles

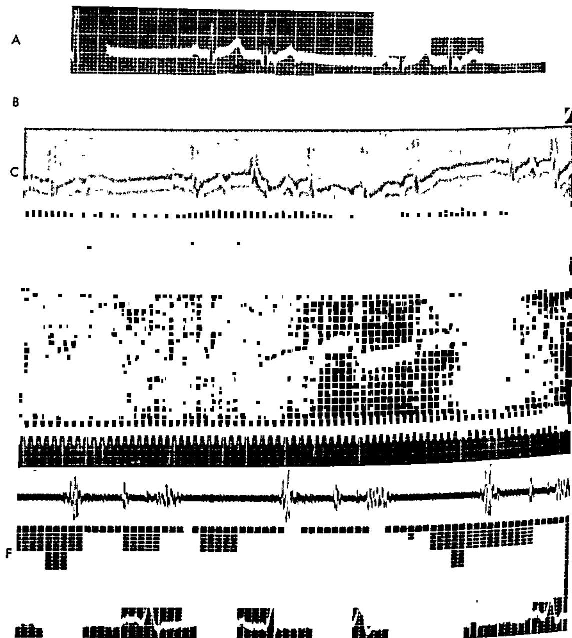


Fig. 11-8. A Lead I. *Nodal or ventricular (?) extrasystoles* with retrograde conduction to the atria, with an inverted P wave between the QRS complex and the T wave B *Atrial extrasystoles in bigeminal groups* with alternation of duration of coupling, and aberration of the QRS complexes of those extrasystoles which have a shorter coupling C. *Blocked atrial extrasystole* at the beginning of the tracing; later, four extrasystoles, with the first conducted to the ventricles with delay and aberration. D *Atrial extrasystoles* with abnormal P wave of the first postextrasystolic beat. E. *AV rhythm* in a dog; lead III. All those beats with an inverted P wave between QRS complex and T wave are followed by a *return extrasystole*. F. Phonocardiogram and lead II of a patient with *bigeminy*. The extrasystole creates only a 1st sound; the 2d sound of the extrasystolic beat is absent.

tressing than the usual ones. It is typical for these sensations to come mostly at rest, which is the time extrasystoles most often occur, chiefly on account of slower rate.

Other patients complain of dizziness or even of *fainting*. Questioning elicits that this dizziness lasts only "a second." The reason for the vertigo in the absence of a long cardiac standstill is not known

Pain is a not infrequent complaint. It may be "knifelike" or stabbing, and its brevity alone speaks against coronary involvement. Often it is not the extrasystole itself which causes palpitation or pain but the first postextrasystolic beat with its larger stroke volume.

Some patients with extrasystoles have a most interesting *cough reflex* The cough appears simultaneously with the extrasystoles, comes from "nowhere," and may be very annoying The mechanism is not clear, but the presence of a reflex from the heart or the pressoreceptors to the respiratory tract is obvious

All these sensations are aggravated if the patient feels his pulse and finds it intermittent.

Signs. Most extrasystoles are diagnosed by auscultation; the heart tones of the premature contraction followed by a pause are heard. However, without an electrocardiogram, mistakes, although rare, can occur, since dissociation with interference, parasystole, or even a periodically dropped beat may lead to a similar auscultatory impression. The 1st sound of the extrasystolic contraction is often accentuated, the 2d sound may be absent (Fig 11-8F)

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Extrasystoles may also give the impression of a gallop rhythm, since the two sounds of the beat preceding the extrasystole are occasionally followed by the only sound produced by the extrasystole

PROGNOSIS

The vast majority of extrasystoles represent a harmless phenomenon Whether they appear singly or in series, occasionally or continuously, even over a period of years, they do not lead to complications and can be ignored. On the other hand, extrasystoles can elicit fibrillation and, if the ventricles are involved, sudden death. This happens when extrasystoles occur extremely early, during the last few hundredths of a second of the T wave of the preceding beat (Fig. 11-12C). If a premature impulse reaches the heart during this phase, the so-called *critical or vulnerable phase*, it leads to rapid firing of impulses resulting in multiple extrasystoles, flutter, or fibrillation. *This does* not happen under normal conditions but occurs when the heart is in an "abnormal metabolic" state, for instance when there is abnormal excitability of a center because of lack of potassium or calcium This is why extrasystoles during chloroform anesthesia and those in acute myocardial infarctions bring so great a potential risk.

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The treatment with drugs is reserved for those patients discussed above in whom the extrasystoles create some risk and for those who complain that the arrhythmia disturbs them The treatment of choice is *quinidine*, which is given three to six times daily in the form of tablets containing 0.2 Gm, after a test dose of 0 2 Gm. Most extrasystoles, but by far not all, disappear with this medication. If hypersensitivity prevents the use of quinidine, one may use *Pronestyl*, 0 75 Gm (three capsules), three to four times daily. While ventricular extrasystoles respond well, the atrial type is less frequently influenced.

The administration of 4 to 8 Gm daily of *potassium chloride* helps, particularly in digitalis-induced extrasystoles, but this therapy is to be used only if renal function is normal, because it carries the danger of other disturbing arrhythmias Digitalis therapy often abolishes extrasystoles not caused by this medica-

disease, patients in private practice) show an incidence of 1.5 to 3 8 per cent.

Factors and Diseases Eliciting Extrasystoles. Extrasystoles may appear *after exercise.* In the majority of such instances, the extrasystoles indicate the presence of myocardial or coronary disease. Actually, the appearance of extrasystoles (usually of varying shape) following exercise should arouse the suspicion of *coronary sclerosis.* Extrasystoles after exercise have been seen in *myocarditis,* and in diphtheria.

Extrasystoles are influenced by *posture.* They are more often found in the supine patient or may be seen only if a patient lies on the left or right side.

They appear in some patients during constipation, menstruation, pregnancy, or with meteorism, in others, after smoking or on sexual excitement. Extrasystoles are common in acute myocardial infarction and in cardiac aneurysms In the former, they seem to originate in the area of reactive inflammation surrounding the infarction. They require therapy with quinidine because of the danger of fibrillation. While extrasystoles are common in diphtheritic myocardial necrosis, they occur less frequently in active rheumatic fever, in spite of the frequent involvement of the myocardium, including the specialized tissue.

Extrasystoles are common in the preexcitation syndrome and in a variety of allergic conditions. They are rare in hyperthyroidism in spite of the frequent occurrence of fibrillation.

Symptoms. As mentioned above, symptoms are present only in a small minority of individuals with extrasystoles, but in some unfortunate ones, the symptoms may be distressing.

Many patients complain of *palpitation.* Only further questioning reveals that this sensation consists in a sudden jumping, skipping, or somersault of the heart, and is not continuous but may repeat itself several times per minute. Interpolated extrasystoles may be more dis-

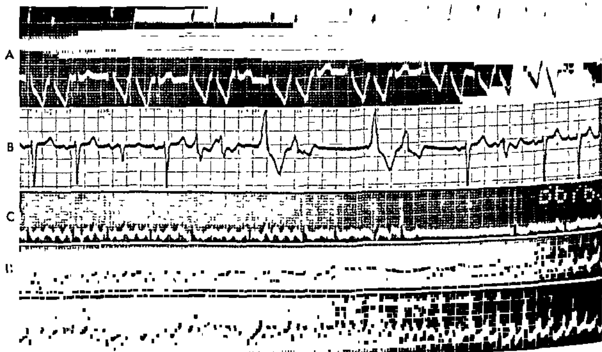


Fig. 11-9. A Lead III in a dog *Trigeminy and multiple extrasystoles* created by focal application of digitoxin to the conus of the right ventricle. B Lead III *Multiple and multiform ventricular extrasystoles and abnormal automatic ectopic beats* in a 72-year-old patient who had received digitalis C. End of an attack of *atrial fibrillation* in a 65-year-old man D Dog, lead II *Atrial flutter* elicited by focal application of aconitine on the tip of the appendix of the right atrium. Cooling of the area of application abolished the flutter and made the sinus rhythm reappear. Discontinuation of the cooling led to reappearance of flutter These results, readily reproduced and confirmed, could not be explained if a circus movement were present. E *Atrial flutter,* elicited in a dog by application of aconitine, is transformed into fibrillation whenever the right appendix is stretched.

4

Flutter and fibrillation

DAVID SCHERF

ATRIAL FORM

Definitions. In atrial flutter, the atrium contracts 200 to 400 times per minute, the movements are *coordinated* and are named after the rapid movements of the wings of certain birds (Fig 11-9D). In atrial fibrillation, the impulses formed in the heart are *more rapid,* so that as they spread over the atria, they meet refractory tissue and coordinated contraction ceases (Fig. 11-9C) A fibrillating atrium gives *the impression of the rippling seen* when a gentle evening breeze agitates the surface of a lake Occasionally the atrial contractions are slightly irregular, so that they cannot be called flutter, while they are not sufficiently irregular for fibrillation A status of *impure flutter* or *flutter-fibrillation* is then said to exist

BRIEF HISTORICAL REMARKS

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for a long time to occur in man That atrial fibrillation is responsible for this common clinical phenomenon was proved for the first time simultaneously by Rothberger and Winterberg (1909) and by Sir Thomas Lewis (1909) Flutter was observed and so named by Williams (1887) but described in man by Jollie and Ritchie (1910)

THE ELECTROCARDIOGRAM

The electrocardiographic picture is easily recognized in atrial fibrillation Instead of normal P waves preceding the QRS complexes, irregularly formed fibrillation waves (*F waves*), with a rate up to 600, are present. *They continuously vary in form* and rate (Fig. 11-9C). The ventricular activity is completely irregular, except in those patients who also have complete AV block. The F *waves are sometimes coarse,* sometimes fine, and may even be invisible in most leads, with the exception of V_1 and V_2 However, the absence of P waves and the complete irregularity of the heart make the diagnosis possible in the last case.

In atrial flutter, the P waves or F waves are regular in form (Fig. 11-10B). They *follow each other like the regular teeth of a saw* with continuous motion, but short isoelectric lines may separate one F wave from another (Fig. 11-9D). *It should be stressed that the form* of the F waves alone differentiates flutter from fibrillation these waves are regular in flutter and irregular in fibrillation (Fig. 11-11).

The ventricular rate and rhythm in flutter show all possible variations. The ventricles may beat rapidly and regularly at a rate greater than 300 per minute when every atrial impulse is conducted to the ventricles (*flutter with full rhythm*). If an intraventricular conduction disturbance coexists or if, because of the rapid rate, the intraventricular conduction is aberrant, a picture similar to that of a ventricular tachycardia appears in the electrocardiogram (Fig 11-10F). More often the arrhythmia is confused with an *atrial paroxysmal* tachycardia (Fig. 11-10C). However, in the majority of cases, the AV conduction system is able *to conduct* only every second, third, or fourth atrial impulse to the ventricles, so that a 2:1, a 3:1, or 4:1 *block* appears (Fig. *11-10B*). *If* the blocking is irregular, the ven-

disease, patients in private practice) show an incidence of 1.5 to 3.8 per cent.

Factors and Diseases Eliciting Extrasystoles. Extrasystoles may appear *after exercise.* In the majority of such instances, the extrasystoles indicate the presence of myocardial or coronary disease. Actually, the appearance of extrasystoles (usually of varying shape) following exercise should arouse the suspicion of *coronary sclerosis.* Extrasystoles after exercise have been seen in *myocarditis*, and in diphtheria.

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Extrasystoles are common in the preexcitation syndrome and in a variety of allergic conditions. They are rare in hyperthyroidism in spite of the frequent occurrence of fibrillation.

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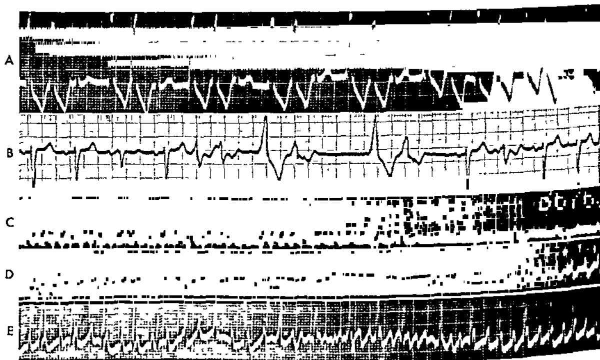


Fig. 11-9. A Lead III in a dog *Trigeminy and multiple extrasystoles* created by focal application of digitoxin to the conus of the right ventricle B. Lead III. *Multiple and multiform ventricular extrasystoles and abnormal automatic ectopic beats* in a 72-year-old patient who had received digitalis. C. End of an attack of *atrial fibrillation* in a 65-year-old man. D. Dog, lead II. *Atrial* flutter elicited by focal application of aconitine on the tip of the appendix of the right atrium Cooling of the area of application abolished the flutter and made the sinus rhythm reappear. Discontinuation of the cooling led to reappearance of flutter. These results, readily reproduced and confirmed, could not be explained if a circus movement were present. E. *Atrial flutter*, elicited in a dog by application of aconitine, is transformed into fibrillation whenever the right appendix is stretched.

the exercise. The original rate is suddenly restored after a few minutes Carotid pressure or any other vagal reflex stops a paroxysmal tachycardia for a longer or shorter time but affects the rate in flutter or sinus tachycardia only while pressure is exerted.

Whether it is permissible to differentiate atrial flutter from paroxysmal tachycardia has been questioned, particularly since rapid firing of impulses is considered to be the responsible mechanism in both conditions The *author believes that these conditions should be separated in spite of certain similarities.* In paroxysmal tachycardias, carotid pressure often abolishes the tachycardia In flutter, this does not happen and actually vagus stimulation increases the flutter rate and causes fibrillation (Fig 11-12B) Many drugs which are effective in abolishing atrial tachycardias are useless in flutter. Atrial flutter is common in cardiac patients and rare in otherwise apparently healthy individuals; the situation is reversed for paroxysmal tachycardias Flutter often changes, spontaneously or after digitalis administration, into fibrillation This is extremely rare in a paroxysmal tachycardia.

CLINICAL CONSEQUENCES

The *ventricular rate* alone is of importance in these abnormal rhythms If with a higher degree of block, the rate is around 80, the patient has an almost normal circulation and may not even notice the restoration of normal rhythm With a rate of about 120, the patient will be handicapped, particularly on undertaking physical exertion With higher rates, cardiac failure, with high venous pressure, hepatic enlargement, fall of the arterial pressure, and cardiac enlargement, will result in direct relation to the rate.

OCCURRENCE

Atrial fibrillation (a more common event) and atrial flutter may occur in apparently healthy people. They may be observed for decades or even during a lifetime without other evidence of cardiac involvement. It is possible that a postinfectious (streptococcic) myocarditis, subclinical and rapidly healed, was originally responsible. We knew one physician who had been refused life insurance because of atrial fibrillation when he was in his twenties; he died at 84, and not from heart disease. The fibrillation never stopped and never required therapy since the ventricular rate remained slow.

In certain lesions, fibrillation is common. It appears sooner or later in most patients with mitral stenosis, hyperthyroidism (which is often masked), or coronary sclerosis. It is rare in cor pulmonale and in many congenital heart lesions. It has been described in healthy young men after severe physical strain. It occurs under certain experimental conditions when the atria are stretched or overfilled (Fig. 11-9E) A high vagus tonus (Fig. 11-12A) and the topical application or intravenous injection of acetylcholine cause flutter or fibrillation (Fig. 11-10E) in the experimental animal. Fibrillation is occasionally seen in a normal dog when the vagus in the neck is stimulated with a faradic current (Fig. 11-12A).

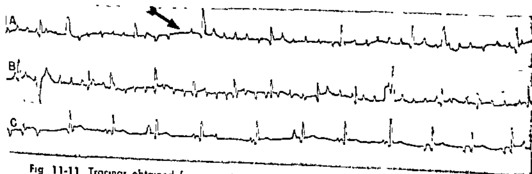


Fig 11-11 Tracings obtained from a patient with shifting of the pacemaker from the SA node to the AV node (C) There is also a change from positive to negative P waves during the presence of flutter This is also explained by two active centers, one in the SA node and one in the AV node, at times, when both centers form impulses simultaneously (arrow in A), an almost isoelectric P wave is obtained.

tion, but one would not give digitalis for such a harmless phenomenon.

MECHANISM

The mode of origin of extrasystoles is known only for the "return" extrasystoles, where one may assume that the impulse conducted in a retrograde way from the ventricles or the AV node to the atria *returns* and "reenters" the ventricles. For the others, the mechanism remains unknown.

There are two main theories. They have in common the assumption that the beat preceding the extrasystole elicits it. The constant coupling of the extrasystoles and the many experiments showing that they disappear when the eliciting beat is inhibited by vagal stimulation prove this assumption to be correct.

One theory, which exists in numerous modifications, assumes *a reentry movement;* it is believed that the impulse, while spreading over the heart, is conducted in a penultimate twig of the conduction system only in one direction with some delay, and that the conduction path is then reentered, thus a second impulse, the extrasystole, spreads over the heart. It must be conceded that these theories are purely theoretical and are not based on experimental facts or clinical observations. There is only one experimental finding, by Schmitt and Erlanger, which is often quoted in support of this theory. The authors believed they had shown that in a small muscle strip, an impulse starting at one end reached the other and then returned to the initial point The authors assumed that the impulse was conducted only in one part of the cross section of the strip (from A to B) so that it could return to A via another pathway. Experiments by Arvanitaki and Bozler have, however, shown that this assumption is incorrect. The impulse traveling from A to B may elicit in one cell at B a repeated firing of impulses and, when a cell becomes depolarized more than once, the second depolarization may spread again over the muscle strip and reach A.

This leads to a second explanation which the author favors· that the *extrasystoles are due to the repeated firing off of impulses.* Normally, when an impulse spreads over the heart, every cell is depolarized once When, because of prolonged negative afterpotential, loss of calcium, or other abnormalities, one cell becomes depolarized *twice* (afterdischarge), a bigeminy appears, since the second depolarization, appearing after the refractory phase of the heart, may form a propagated impulse. A similar phenomenon has been demonstrated for various types of nerves, and its occurrence was proved in the heart muscle of experimental animals If a long series of depolarizations follows (*repetitive response*), the patient has one of several forms of paroxysmal or ectopic tachycardia.

incidence of fatalities increases if larger doses are administered. Patients have died *from* ventricular fibrillation or respiratory *standstill or* systemic embolism. Thus, the patient is exposed to *a not inconsiderable danger* without too great a benefit *In most* patients with mitral *stenosis*, the dilated left *atrium* fails anyway to *contribute to the dynamics of the circulation* In *any* case this therapy should *always be carried* out only in a hospital, for *continuous supervision of the* patient *is* essential. The second chief reason against this therapy *is* that, *in* most patients (actually in almost all of them *if they* suffer from rheumatic heart *disease or* coronary sclerosis), fibrillation *reappears and often is again* present within a few days after therapy is discontinued In order to avoid embolism, it is recommended that an anticoagulant be given for 14 days prior to the quinidine therapy, so that thrombi already *present* will have time to adhere to the wall and no new ones will form.

Experience shows that with any method of administration of *quinidine*, one succeeds in reestablishing sinus rhythm in about 80 per cent of the patients At first, a test dose of 0 2 Gm is given in order to determine whether there is hypersensitivity. On the next day, 0 2 Gm is given every 2 hr from 8 A.M. to 8 P.M., or 0 4 Gm every 4 hr day and night The success is the same with both procedures If no result is obtained, the single doses may be increased, but this is recommended only under close supervision, since the risks are increased In recent years, frequent use of quinidine therapy for interruption of fibrillation has been recommended without good reasons.

Flutter. In this condition, treatment is usually required and is more difficult It is more often necessary because only exceptionally does the patient with flutter have a slow ventricular rate at rest and with the ordinary exertions of daily life The rate is usually too high and the circulation deteriorates The therapy is more difficult, since in most cases the administration of digitalis in the usual dosage does not inhibit AV conduction and cannot thereby slow the ventricular rate. The slower impulses of flutter are less inhibited on their way to the ventricle than the faster impulses of fibrillation

Since flutter is transformed *into fibrillation by large doses of digitalis*, one can prescribe *from the beginning about* 0.5 mg *digitoxin* daily, and *in most* patients will succeed within *a few days* in transforming the flutter into *fibrillation*. When this *is* accomplished, the continuous *administration* of small maintenance doses of digitalis will keep the rate down; sometimes fibrillation changes spontaneously *into* sinus rhythm. Some authors prefer to start with *quinidine* at once without using digitalis, the dosage being the same as in atrial fibrillation. If quinidine is used in flutter or fibrillation, a paradoxic *phenomenon is common*, viz, an increase of ventricular rate. *This* is explained by the atropine-like action of quinidine on the vagus endings, which appears even with the use of ordinary clinical doses. *There* are, however, *instances of atrial* flutter in *which digitalis therapy* does not change the existing rhythm, despite the largest tolerated doses, and in which quinidine also fails. In such cases one must abandon treatment and try again after a few months.

VENTRICULAR FLUTTER AND FIBRILLATION

Ventricular flutter has been described repeatedly, but no accepted rules exist on its separation from rapid ventricular paroxysmal tachycardia (Fig. 11-10D). As in atrial flutter, the rate may be decisive. It may, in the dog, reach 500 or more.

Ventricular *fibrillation* is one of the most common causes of sudden death, for the circulation stops (Fig. 11-12C). It *is often survived* in the cat and in small mammals, since in them it stops spontaneously. This happens only rarely in man. It has been seen in complete heart block in coronary sclerosis, particularly when quinidine is being given Ventricular fibrillation is a not uncommon cause for fatal accidents during administration *of anesthesia*, particularly with *refrigeration* of the heart.

Of interest *is the ventricular fibrillation* which *appears after prolonged hyperventilation* with resulting *hypocapnia. A rise in* serum potassium and a fall *of potassium in the* heart *muscle seems to be responsible*. Two methods are available *to eliminate it* and to revive a patient with ventricular fibrillation. One is the old method of Prevost and Bacelli, who recommended strong electrical shocks. Through the *efforts of Zoll* (1952), relatively simple de-

tricles may show the same *complete arrhythmia* as in fibrillation. If there are 4:1 and 2:1 blocks alternating regularly, a *bigeminal rhythm* caused by extrasystoles may be diagnosed on auscultation.

CLINICAL DIAGNOSIS

This is easy in *fibrillation* because of the complete irregularity of the heart. Confusion with irregularly placed extrasystoles may occur and is fatal if the series of irregularly grouped ventricular extrasystoles seen in digitalis intoxication is confused with atrial fibrillation with a rapid ventricular rate, and if the physician, without the help of an ECG, decides that the patient needs more digitalis. In doubtful cases one may be aided by the knowledge that extrasystoles usually disappear after exercise or the inhalation of amyl nitrite while the irregularity of fibrillation increases with these measures

The clinical diagnosis of *atrial flutter* is possible in most instances. A fundamental clinical rule should be that every regular heart activity with a rate of 100 to 160 per minute should arouse suspicion of flutter with 2:1 or 3:1 block. In sinus tachycardia, the rate increases with the patient standing or performing moderate exercise, and gradually returns to its former level with rest. In flutter, as well as in the paroxysmal tachycardias, the rate remains the same. However, more strenuous exercise causes change of block, so that a 3:1 block changes into a 2:1, or the latter into full rhythm, there are characteristic mathematic relations between the rate prior to and after

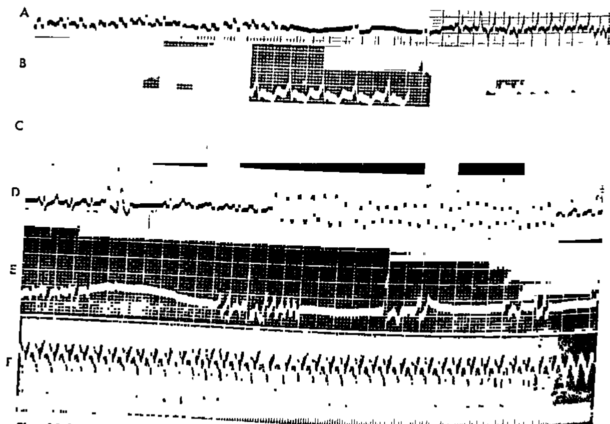


Fig. 11-10. A *Atrial flutter,* caused in a dog by focal application of aconitine, is immediately abolished by cooling the area of application Two sinus beats appear. Discontinuation of the cooling leads immediately to atrial fibrillation B The three standard leads. *Atrial flutter* with 2 1 block. C The three standard leads. *Atrial flutter* with complete AV conduction; these tracings are readily confused with paroxysmal atrial tachycardia D. *Paroxysmal ventricular flutter* appearing during cooling of a small area of the right ventricle of a dog E. *Sinus standstill* and short attacks of *atrial flutter* immediately following focal application of acetylcholine on a dog's atrium. F. Lead III of a man with *paroxysmal tachycardia;* further analysis of many tracings, taken over a period of weeks, revealed that the condition under investigation was *atrial flutter* and *aberrant intraventricular conduction.*

5

Pathologic findings in disturbances of rate or rhythm

ANTONIO COSTA

SINUS BRADYCARDIA

A possible cause of sinus bradycardia is *arteriosclerosis* of the artery which supplies the SA node (Fiorio), followed by fibrosis of the nodal tissue Caution should be taken in the evaluation of the pattern, because similar lesions have been considered responsible for paroxysmal tachycardia (*Doerr*). A *congenital* absence of the SA node has never been observed, *even in malformations* of the superior vena cava Theoretically, this would cause a slow pulse due to nodal rhythm.

ATRIAL FIBRILLATION

It is difficult to find a correlation between atrial fibrillation and atrial lesions of rheumatic, sclerotic, or toxic nature On the contrary, it is more likely that, in accordance with Prinzmetal's concept (1951), there is an ectopic focus, generally in the posterior wall of the right atrium, represented by an area of intact myocardium within the rest of the degenerated tissue

ATRIOVENTRICULAR BLOCK AND BUNDLE BRANCH BLOCK

The pathologic findings in cases with disturbances of conduction are by no means concordant According to Bach, Pardee, Laubry, etc, the electrocardiographic pattern of block can be found in patients in whom histologic sections fail to disclose lesions of the conducting bundles This possibility, however, is denied by others (Beretta and Maestrelli), who found alterations in all the cases submitted to study Even in the so-called "functional blocks," structural lesions of the conduction system should be admitted, in addition to functional disturbances (Fig 11-13). Several authors, on the other hand, deny that a localized or diffuse damage of the cardiac muscle can determine a pattern of bundle branch block without simultaneous lesions of the conducting system (Scherf, 1925, Laubry et al., Smith, 1932, Robinson).

Transient or *functional block* is often due to minor lesions of the branches that may escape *even an accurate study On the other hand,* diffuse degenerative or sclerotic lesions of the *AV node and bundle of His have been described without the occurrence of specific electrocardiographic* pattern of block

According to Monckeberg, failure to demonstrate lesions of the bundle of His in typical cases of block may be explained by (1) incomplete histologic examination of the conducting system, (2) lesions of the neurologic components of the bundles, (3) existence of anatomic abnormalities, such as anastomoses between the two branches

The value of a *functional factor* was overestimated in the past but still should not be *altogether disregarded.* A lesion of a small area of the conducting system may become "functionally" total because of compression and stretching of the other fibers Serial histologic studies have shown an *interruption of the*

THERAPY

Fibrillation. It has been stressed that the ventricular rate alone is responsible for the disturbances caused by flutter and fibrillation. Actually, in fibrillation the atria do not contribute to cardiac dynamics as they are practically paralyzed, and with the disappearance of sinus rhythm, venous and atrial pressures rise, even when the ventricular rate during fibrillation was slow. This does not hold true, however, for all patients, and it must be stressed that fibrillation may persist for many decades without the patient's being handicapped in any way, provided the ventricular rate is slow.

The chief therapeutic problem is to slow down the ventricular rate, and this is often accomplished by *digitalis*. This is, however, a purely symptomatic form of therapy. Patients respond to it readily unless complications such as hyperthyroidism, active rheumatic fever, or pulmonary embolism exist. Once the ventricular rate is below 80 beats per minute, a maintenance dose will keep it at this level.

Only rarely should an attempt be made to eliminate fibrillation. This is recommended when hyperthyroidism is cured but fibrillation persists; if fibrillation appears during pneumonia or some other infectious disease and does not disappear spontaneously; or when fibrillation has just started in slight mitral stenosis and a loud presystolic murmur indicated earlier that the left atrium still contributed to ventricular filling. In the vast majority of cases defibrillation is not indicated. Several independent investigators have found that *quinidine* therapy causes death in 4 per cent of the cases, even when doses of not more than 1.5 to 2.0 Gm are given daily. The

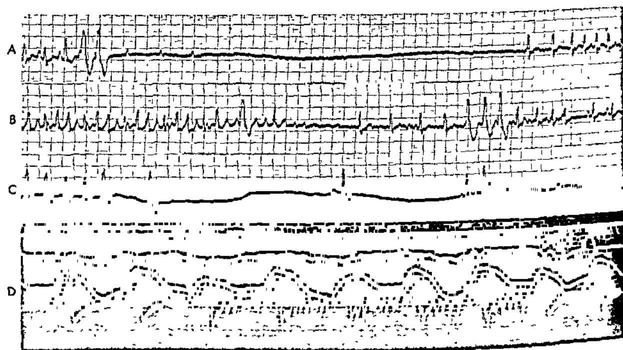


Fig. 11-12. A and B are continuous Lead III, dog experiment. The animal had received veratrine before, and parts of the SA node had been crushed by a clamp. In A, *atrial fibrillation* appears during faradic stimulation of the right vagus nerve in the neck. When this fibrillation changed into flutter, a repetition of the vagus stimulation led immediately to fibrillation. Sinus rhythm reappeared on termination of the second vagus stimulation. C. Dog experiment; veratrine, applied locally to a small area of the outflow tract of the right ventricle, had led to the appearance of ventricular extrasystoles. Cooling of the area of application led to the disappearance of the extrasystoles. There is *cardiac standstill*, presumably because the rapid extrasystoles were retrogradely conducted to the atria and inhibited the SA node. The first sinus beat is followed by an *atrial extrasystole*, which, reaching the ventricle during its critical, or vulnerable, phase, elicits *ventricular fibrillation*. D. Dog experiment. Lead from anus to esophagus. *Complete AV block* existed after severing both bundle branches. The top line represents a signal, the second a mechanogram of the right atrium, and the third a mechanogram of the right ventricle. One short electrical shock (signal) leads to a short attack of *atrial fibrillation*.

Vascular, inflammatory, and degenerative lesions may affect the conducting system either with the rest of the myocardium or as an isolated process (Fig. 11-14). The *vascular changes* are characterized by *small hemorrhagic areas* favored by the rich vascularization, and by areas of degeneration. AV block or bundle branch block has been often observed in the course of a myocardial infarct Mahaim (1928) and Hochrein have described the frequency and causes of this condition

In general, it is admitted that the bundle branch block which appears in cases with coronary arteriosclerosis is due to lesions of either one or both of the branches According to Mahaim, the occlusion of the anterior descending branch causes *right bundle branch block* or *AV block* Actually, the AV node, the bundle of His, and its right branch receive their blood supply from this arterial branch On the contrary, left bundle branch block appears when the right coronary artery is also occluded Many authors (among them Hochrein) have accepted this viewpoint, which is not accepted by Master and coworkers

Among the *inflammatory processes*, acute interstitial myocarditis, rheumatic nodules, and purulent myocarditis have been described Small abscesses of the conduction bundle should be considered as a result of diffusion of the inflammatory processes to the bundle through the endocardium, less often they are caused by a shower of mycotic emboli, as in a case of Mahaim.

AV block is an important complication of diphtheria and reveals the existence of severe myocarditis.

Generally, the AV block, which is frequently observed in *many infectious processes* (pneumonia, scarlet fever, influenza, mumps, rubeola), is not accompanied by specific lesions of the conducting system; the block is likely to be caused chiefly by action of toxins on the AV node and the conducting bundles. Such a toxic-infectious process may explain the AV block observed in the course of *rheumatic fever* and *diphtheria* without focal lesions [1] In some of these cases, albuminoid, hyaline, fatty,

[1] A toxic process may be such as to be inapparent upon routine histologic examination while it might be revealed by more refined studies of histochemistry. *Editor.*



Fig. 11-14. A SA node. hyperplasia of the elastic tissue in the wall of the nodal artery. B. Thickening of the wall of the nodal artery in a patient with pentalogy of Fallot. C. Left branch of the bundle of His. isolated fibers of the conductive system surrounded by thick fibrotic tissue.

waxy, or vacuolar degeneration has been observed

Specific granulomatous processes have been observed in addition to more common inflammatory lesions, these processes were particularly described in cases of *syphilitic* or *tubercular myocarditis*

Syphilis is an uncommon cause of AV block. However, the conduction disturbance may be due to a gumma infiltrating the bundle of His or both branches, to gummatous myocarditis spreading from the aorta, or to an aortitis causing narrowing of the coronary mouths.

In cases of *calcific aortic stenosis*, different

vices are now available for this purpose and permit stimulation of the heart even with an unopened chest. The other method is rapid exposure of the heart by a large incision in the fourth intercostal space; intracardiac administration of procaine; massage, and administration of oxygen. The latter is done by intratracheal tube or mouth-to-mouth breathing if no tube is available, for quick action is urgent; the cortical centers are very sensitive to lack of oxygen and are damaged if the circulation is arrested for more than 3 min.

Mechanism of Origin. The mechanism of flutter and fibrillation in the atria or ventricles has long been unknown, but recently additional data have been brought forward favoring one of the existing theories. For more than 65 years flutter and fibrillation were explained by rapid impulse formation in one or several centers in the atria or ventricles respectively. There are many modifications of this theory based on experimental evidence. The centers were located in the SA node, in the AV node, or both. These theories were practically abandoned when the *circus movement* theory was developed, mainly by Lewis (1916) and Garrey. Lewis based his work on previous experiments by Mines and Romanes and assumed that a "circus" or "reentry" wave moves *up or down the SA node and follows a circular* pathway, from this "mother" or "central" wave, the rest of the heart is excited by centrifugal excitation waves. This fascinating theory was generally accepted, and even in textbooks of physiology it was "the" explanation; in some it still is. This was mainly because of the very elaborate and well-arranged experiments of Lewis, which seemed to be convincing. Objections to his theory were raised many years ago but were disregarded. Thus, Rothberger pointed out (1922) that the two fundamental experiments, one in the dog and one in man, which Lewis considered crucial in proving the existence of a circus movement, were actually open to serious criticism Even the existence of a circular path in this area still lacks anatomic proof, and the use of the whole path by a circus wave has never been demonstrated. If this wave were present, broad ligatures across the path should stop electrically induced flutter, but they do not, as demonstrated by the author (1928).

Lewis himself stressed that his theory cannot explain ventricular fibrillation and that this constituted a serious weakness because of the identity of the atrial and the ventricular form. Ventricular fibrillation was explained by Garrey's hypothesis, which is based on much less experimental data than the theory of Lewis.

Experiments of the author and his coworkers have shown that atrial (Figs. 11-9D and 11-10A) and ventricular flutter and fibrillation (Fig. 11-10A) can be caused by topical application of *aconitine*. Other experiments demonstrated that atrial flutter can, in this way, be caused by rapid impulse formation in one center; that atrial fibrillation can be evoked by rapid impulse formation in one or several centers, that ventricular flutter can originate from rapid firing of impulses in one center. There is no proof of the mechanism of ventricular fibrillation, but the activity of several centers is probable. It is assumed, on the basis of experimental data, that rapid impulse formation in one center induces rapid impulse formation in others, as this relationship has been known for a long time to exist in the nervous system.

Since the existence of at least two forms of fibrillation of the atria causing identical electrocardiographic patterns has been proved, viz., the arrhythmia arising in one or in several centers, other forms may exist. There is, however, no proof that a "circus movement" may be responsible, if it occurs locally, it may well be merely the consequence of rapid impulse formation and the appearance of islands of refractory tissue. If this is the case, it would be maintained by fibrillation but would not sustain it.

6

Sinoatrial and atrioventricular blocks

SAMUEL BELLET

SINOATRIAL BLOCK

General Features. In sinoatrial *(SA) block*, there occurs a sudden decrease in the heart rate, usually to almost half the previous normal rate, which may last for one cycle, several cycles, minutes, or hours. This decrease in heart rate can be explained on the basis of an actual physiologic block occurring within or around the structure of the SA node and preventing conduction of the impulse to the atria. This sudden halving of the heart rate is usually preceded by a slight speeding up of the heart and is followed by cycles which are slightly longer but which then gradually shorten until the usual cycle is reestablished. Both the atria and ventricles participate in the irregularity (Fig. 11-15). The heart rate may be as slow as 30 to 36 beats a minute. This condition should be differentiated from other types of slow heart action, particularly sinus bradycardia and various degrees of AV block.

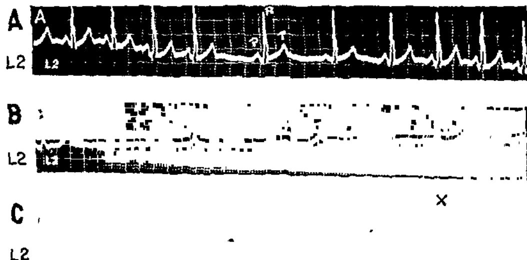


Fig 11-15 A Sinus arrhythmia. Note the phasic variation of the R-R interval. The rate increases during inspiration and becomes slower during expiration. The shorter cycles are associated with a decreased T-P *interval. The P-R interval* remains constant throughout. B Sinus bradycardia. Both the atrial and ventricular rates are slow (34 *per minute*), and the P-R interval is normal. C. Note the presence of a normal sinus rhythm with a rate of 75 per minute. *In the last cycle* (marked X) a long pause is observed. The cycle length of the long cycle is slightly less *than that of two normal* cycles. This constitutes a *SA block* (occasionally the R-R interval of the long cycle is exactly *equal to that of two normal cycles*).

branches in all cases of block clinically diagnosed

The localization of the lesion in cases of bundle branch block has been the object of numerous studies, because for a long time, there was no agreement between the findings and the ECG pattern. In most observations, the alterations involved both branches, even though one of them was generally more injured than the other. However, the reversal of opinion due to the school of Wilson finally reconciled the clinical interpretation with the pathologic findings. On the whole, few cases of bundle branch block have been studied histologically and the technique used is not always above reproach Mahaim (1928) emphasized the need for serial, uninterrupted sections of the bundle of His and its branches. His conclusions were as follows:

1 In bundle branch block, the lesions are usually bilateral, even though one of the branches shows more severe damage

2. The branch with the worst lesions is usually that which had been suspected on the basis of electrocardiography.

3. Right bundle branch block is most often due to a lesion of subdivisions of the anterior descending branch of the left coronary artery.

4 Left bundle branch block, as a rule, is not caused by ischemic factors because of its dual blood supply. It is usually caused by an inflammatory process which spreads from the valves to the septum and from there to the left branch. These conclusions are not completely above criticism but give an idea of the complexity of the problem.

It is interesting to mention that extensive lesions of both branches have been found without typical ECG patterns of bundle branch block (Yater, 1938). This might be explained by the existence of a few intact fibers, still able to conduct the stimulus. Therefore, it shall be concluded that the most important point is the localization of the lesion and not its nature

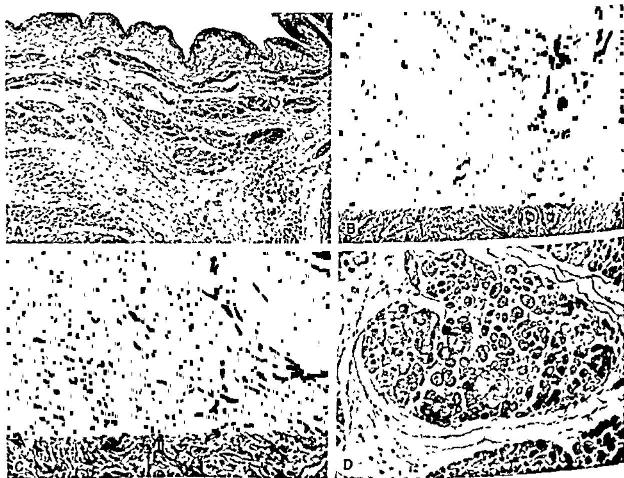


Fig. 11-13. A Rheumatic myocarditis Aschoff nodes near the left branch of the AV bundle. B SA node; moderate hyperplasia of the connective tissue C. SA nodes; severe hyperplasia of the connective tissue. D. Right branch of the bundle of His. degenerative phenomena of the conducting fibers.

heart; *dizziness* and *faintness* may *occur* if the sinus pauses are prolonged.

Diagnosis. The diagnosis of SA block may be suspected clinically but can best be made by means of the electrocardiogram.

Electrocardiogram. In the electrocardiogram, there is a pause or series of pauses, each one of which is slightly *less than double the normal* P-P interval, *occasionally, the pause is exactly equal to that of two normal cycles.* Both the atrial and the accompanying ventricular *complexes are lost* during the pauses (Fig 11-16) *The duration* of the SA block may vary as follows, (1) the irregularity may be observed for a few cycles, (2) the rate may be *suddenly halved, dropping,* for example, from 75 to 38 per minute—*this slow* rate may persist for several minutes or longer, (3) *the disturbance* may be present for long periods of time *and may be the* underlying mechanism for long-continued bradycardia

Because SA and AV block are due to somewhat similar factors, it is not surprising that these two irregularities are *frequently* associated

Treatment. No treatment is required in the absence of symptoms *or signs.* However, when the sinus rate drops to a low *figure* with the *resultant production* of syncopal attacks (more common *in* the *older* age group), it is advisable to administer certain drugs *to diminish* or *eliminate* vagal tone, e g , Isuprel, 10 mg, sublingually, *ephedrine* sulfate, ⅜ gr (25 mg) three times a day, or *other sympathomimetic drugs or* atropine sulfate, or Banthine Drugs which would increase vagal tone, such as Prostigmine or digitalis, should be omitted or used with caution Toxicity due to quinidine, procaine amide, or potassium, which *may* be an additional causative factor, should be appropriately treated

PROLONGED SINUS PAUSES (CARDIAC STANDSTILL) AND ATRIOVENTRICULAR NODAL ESCAPE

If, for any *reason,* the SA node fails to *initiate* the cardiac impulse, the *AV* node, because it also possesses the property of rhythmicity to a *degree only* slightly below that of the SA node, soon "*escapes*" and initiates the heart *beat* It maintains a slow *and regular* rhythm until the SA node can again resume its *function* as the pacemaker. *Ordinarily,* the AV node is prompt to assume its pacemaker function In certain instances, however, this assumption may be *delayed,* with the result that there is *complete cardiac standstill. This asystolic state may* be of sufficient *duration* to produce dizziness or even *syncopal attacks.* Such pauses are the result of vagal effects which may occur spontaneously as a result of reflex disturbances *or may be produced in* susceptible individuals by *carotid* sinus pressure. These seizures usually respond to atropine or ephedrine *If the AV* node fails to take over the role of pacemaker, a ventricular center, usually located in the *upper portion* of the interventricular septum, may assume this role. This phenomenon is called "ventricular escape" *If the periods of* cardiac standstill are unduly *prolonged* because of failure of the AV node or an idioventricular *center to* assume temporarily the role of pacemaker, cardiac arrest or ventricular fibrillation ensues. Such episodes *are particularly* apt to occur as the result of depression of *the conducting* tissue by anesthesia, hypoxia, potassium, *or* full doses of quinidine or procaine amide.

WANDERING PACEMAKER BETWEEN THE SINOATRIAL AND ATRIOVENTRICULAR NODES

Under conditions of increased vagal tone, the rhythmicity of the SA *node becomes* reduced and that of the AV node remains the same or *increases* somewhat. Consequently, the function of the *pacemaker* shifts to the AV node. With a subsequent *decrease* in vagal *tone, the* pacemaker returns to the SA *node. As seen on the electrocardiogram,* this *shift* is *not sudden but occurs over a space of several beats* Progressive changes *are seen* in the P waves *during* the shift They undergo *change* in size, *shape, and direction* simultaneously, with a shortening of *the* P-R interval until the *classic* "high nodal" pattern is achieved (inverted P wave with a P-R interval of less than 0.10 sec) With a *return* of the pacemaker *to* the SA node, these changes occur in reverse. At times, P waves, transitional *in form,* are observed They *are* thought to be due to the simultaneous firing of the SA and AV *nodes.* Since the shift of pacemaker function is not abrupt, *there must* be a phase in which each node has partial *pacemaker* activity, *and* thus *two impulses* traverse the *atrial* muscle in op-

degrees of AV block may be caused by the spreading of the calcific process from the aortic ring to the conduction tissues in the ventricular septum.

Fiorio and Marino studied the alterations of the AV system in *experimental thyrotoxicosis*, and observed degenerative lesions consisting of sclerosis and calcification of the system, with its partial or total interruption. Less frequently were noted atrophic phenomena caused by compression of calcium deposits at the level of the trigoni fibrosi.

Primitive and secondary tumors may cause the interruption of the conducting system (Mahaim, 1928). Nagayo described a primary leiomyoma of the branches, and Monckeberg, a lymphangioendothelioma of the AV node. *Fetal and neonatal fibroelastosis* may cause interruption of the bundle of His and its branches (Mahaim, 1928).

Congenital AV block is considered by Yater and coworkers as due to a septal defect or to a defect in the development of the conductive tissue. Histologic studies have shown in some cases a separation between the AV node and the bundle of His caused by a fibrous nucleus. This lesion is, however, very rare.

In a study on the conducting system in congenital heart diseases, Costa and Fiorio observed that the defects of the septum membranaceum have little importance in regard to the disposition and structure of the adjoining conduction system. Defects of the interventricular septum, on the other hand, are often associated with disturbed growth of the bundle of His resulting in poor development and abnormal course of the left branch.

THE WOLFF-PARKINSON-WHITE SYNDROME

The Wolff-Parkinson-White syndrome is apparently caused by an abnormal and specific lesion in the atrium or near the AV node, the hypothesis of an aberrant bundle has never been documented by serial histologic studies[2] Katz, in one-half the cases with this syndrome, observed the existence of heart disease of either inflammatory (rheumatic, syphilitic, etc.) or degenerative type

The most common pathologic findings are interstitial edema, vacuolar degeneration of the myocardial fibers, chronic rheumatic myocarditis, and scars near the AV node.

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